The American Journal of

CARDIOLOGY

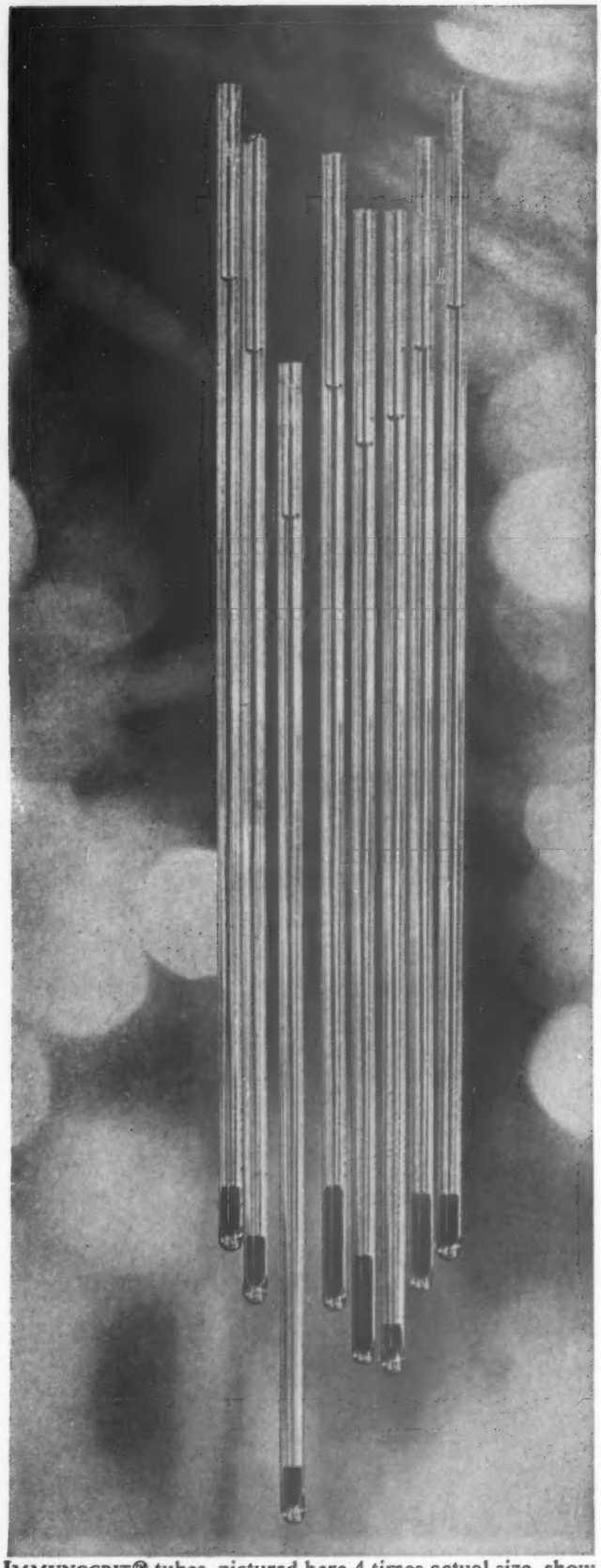
OFFICIAL JOURNAL OF THE American College of Cardiology

Racial Incidence of Coronary Disease

Pathologic Anatomy of Mixed Levocardia

A PUBLICATION OF THE Yorke GROUP

AUGUST 1961



IMMUNOCRIT® tubes, pictured here 4 times actual size, show results of centrifuging patients' serums with BETA-L TEST antiserum. Longest columns of precipitate indicate high beta-lipoprotein levels.

NEW...

A SPECIFIC SIMPLE INEXPENSIVE TEST FOR ESTIMATING SERUM BETA-LIPOPROTEIN LEVELS

BETA-L TEST™

The growing evidence implicating beta-lipoprotein as one of the agents responsible for atherosclerosis has emphasized the need for a test procedure which is reliable, yet simple enough to be suited to clinical purposes.[1] Hyland BETA-L TEST answers this need. BETA-L TEST results show a close correlation with complex quantitative methods now in use, yet BETA-L TEST can be performed in ten minutes on one drop of serum and employs a minimum of laboratory equipment and technical skill.[2]

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When ordering your next beta-lipoprotein determinations, specify Hyland BETA-L TEST. Materials for BETA-L TEST are now available to your laboratory in 60-test kits.

1. Wood, F. C., Gurin, S., and Kuo, P. T.: Medical Correlation Clinic on Atherosclerosis and Coronary Artery Disease, Am. Pract.–Dig. Treat. *12:* 235 (April) 1961.
2. Heiskell, C. L., Fisk, R. T., Florsheim, W. H., Yachi, A., Goodman, J. R., and Carpenter, C. M.: A Simple Method for Quantitation of Serum Beta-Lipoproteins by Means of the Immunocrit, Amer. J. Clin. Path. *35:* 222 (March) 1961.

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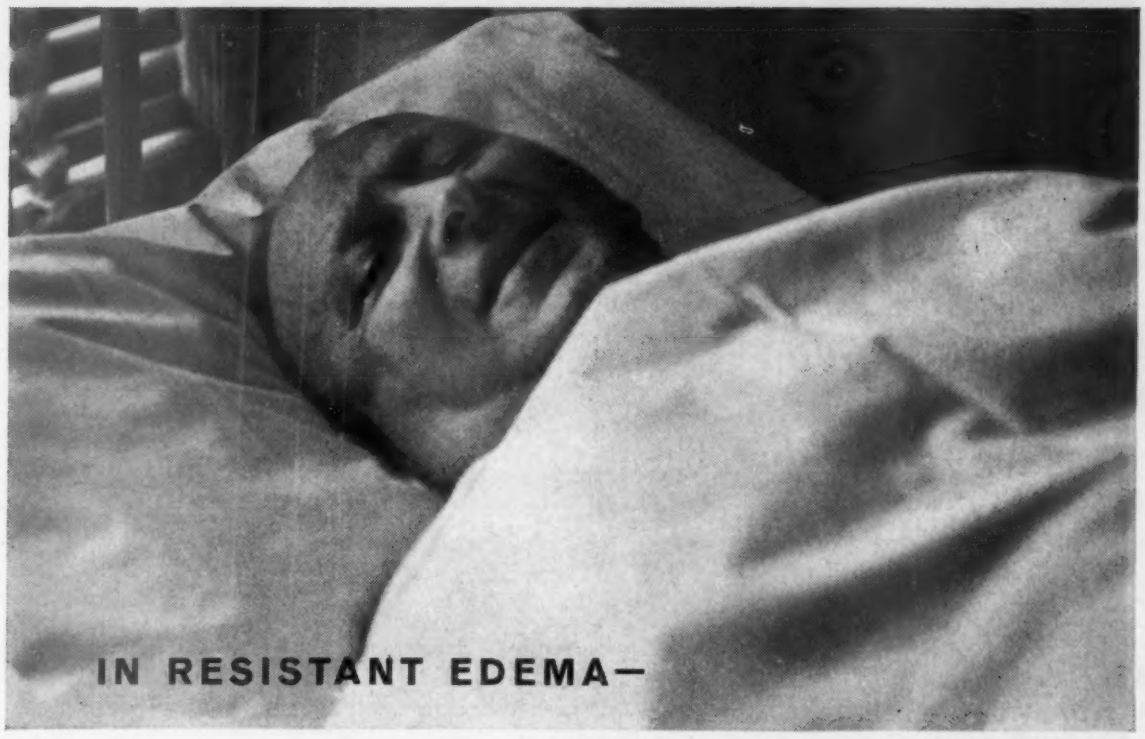

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(brand of spironolactone with hydrochlorothiazide)

● restores dry weight ● ambulates the patient

When patients require maximal control of edema and ascites, Aldactazide will frequently free them from excess fluid when no other drug or combination of drugs will do so adequately.

The two components of Aldactazide—Aldactone®, brand of spironolactone, and hydrochlorothiazide—activate diuresis by two different mechanisms in two different sites of the renal tubules. This separate and dual influence increases diuresis not merely by additive but by truly synergistic increments.

Further, by protecting potassium reserves, Aldactazide provides optimal safety when therapy must be prolonged.

With Aldactazide many of your patients can lead more normal lives, in greater comfort with less restricted activity, free from the burden of edema and ascites.

INDICATIONS:

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Aldactazide is supplied as compression-coated white tablets, each tablet containing 75 mg. of Aldactone and 25 mg. of hydrochlorothiazide.

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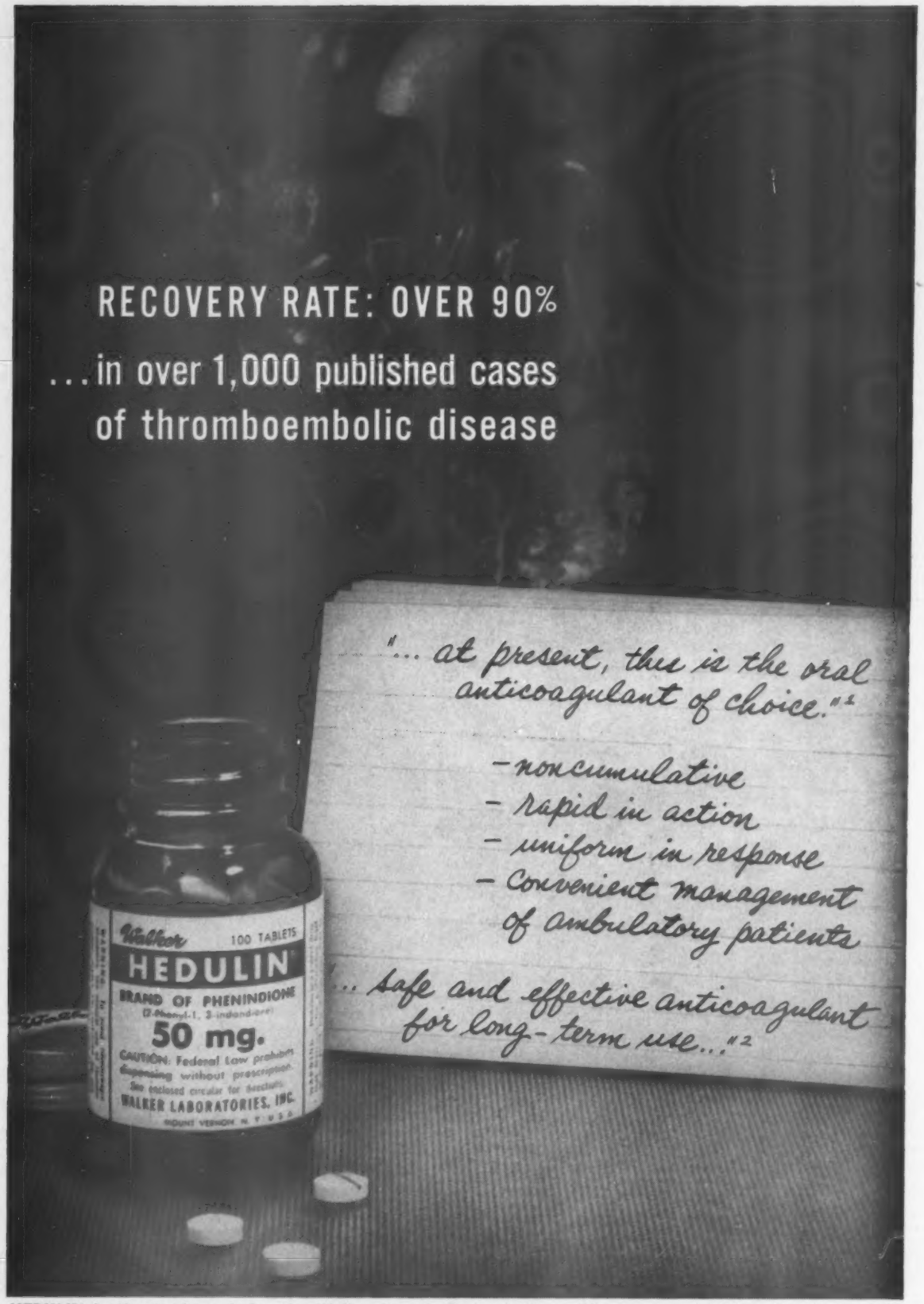

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1. Breneman, G. M., and Priest, E. McC.: Am. Heart J. 50:129 (July) 1955. 2. Tandowsky, R. M.: Am. J. Cardiol. 3:551 (April) 1959.

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The American Journal of Cardiology

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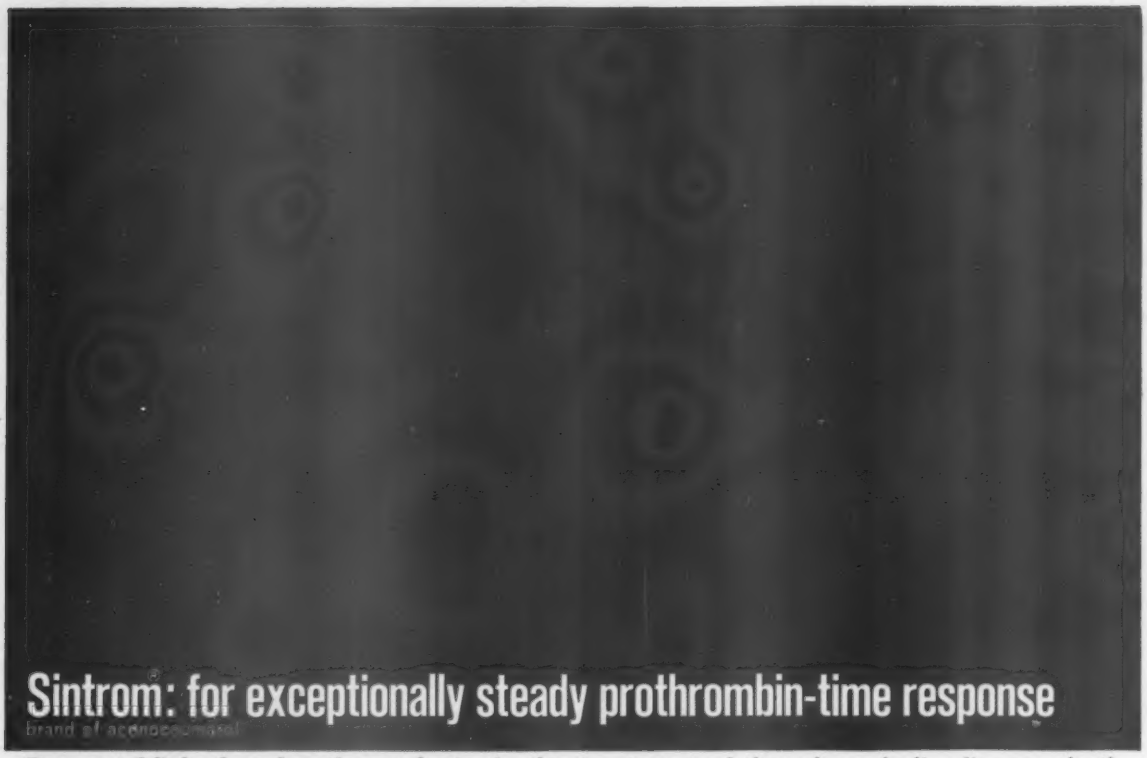

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Distinguished by high potency and its ability to maintain a uniform response with a constant single daily dose, Sintrom is particularly suited to long-term therapy. Significantly more rapid and transient in action, Tromexan is well adapted to cases calling for more immediate control of thrombotic tendencies.
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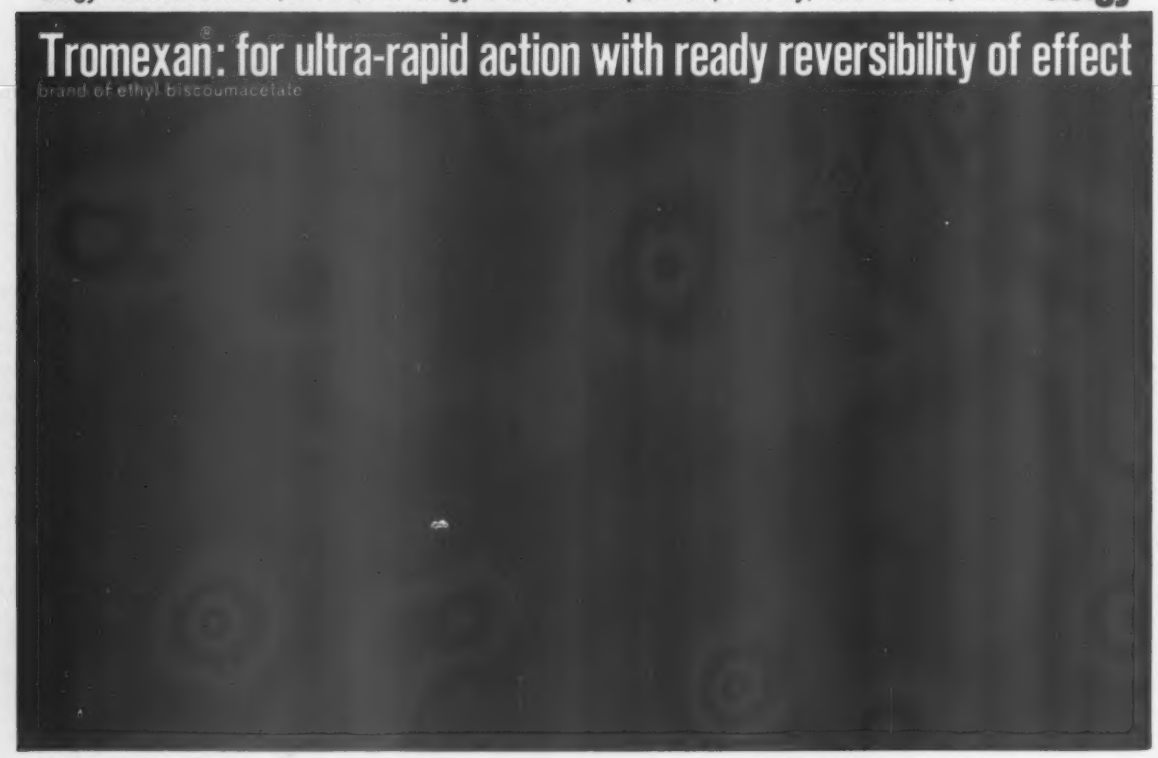

The American Journal of Cardiology

Volume VIII AUGUST 1961 Number 2

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Clinical Studies

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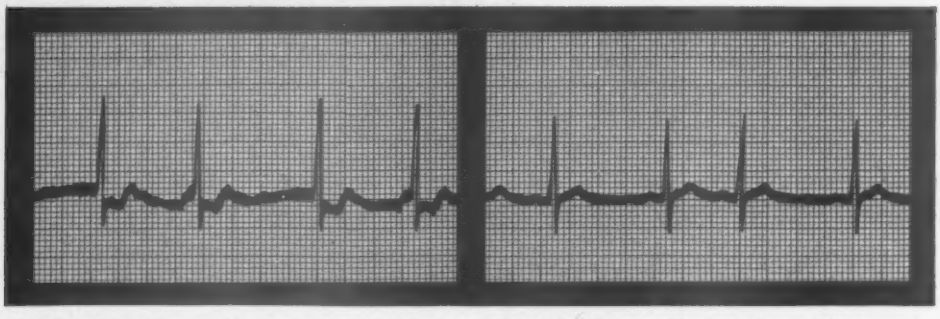
coronary artery disease is not limited to angina

...neither is Peritrate

In postcoronary patients with or without angina, Peritrate provides the benefits of substantial and sustained increase in myocardial blood flow without significant change in cardiac output, blood pressure or pulse rate.

electrocardiographic evidence in

a patient [with] angina*

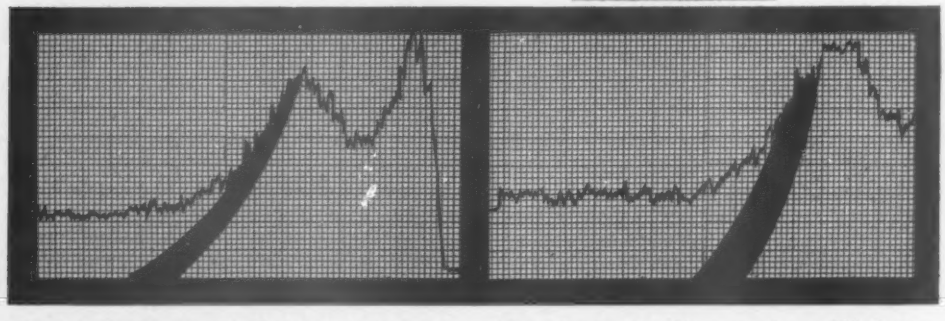


Before Peritrate—S-T segment depressed after standard exercise.

After Peritrate (20 mg. given 4 hours before exercise test) S-T segment now normal.

radioisotopic tracings of

a postcoronary patient [without] angina*



Before Peritrate—Radioisotopic tracing shows reduced myocardial blood flow (shaded area) after infarction.

After Peritrate (20 mg. given 2½ hours before study) myocardial blood flow substantially increased.

Full dosage information, available on request, should be consulted before initiating therapy.

***Electrocardiograms, radioisotopic tracings and case histories on file in the Medical Department, Warner-Chilcott Laboratories**

basic therapy in coronary artery disease
—with or without angina

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brand of pentaerythritol tetranitrate **makers of Tedral Gelusil Proloid Mandelamine**

Watch your mail for ECG Interpretation Series

CONTENTS continued—August 1961

VOLUME EIGHT NUMBER TWO

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Brand of piminodine ethanesulfonate *ethanesulfonate*

An analgesic for

1. Ambulatory patients.

Whenever codeine or codeine-aspirin combinations are used, Alvodine taken orally can relieve pain better without dulling mental acuity or enervating the patients.

2. Postoperative patients.

Alvodine injected parenterally is as potent as morphine, but unlike morphine, it permits patients to remain alert postoperatively. It favors early mobilization of patients because it is usually not hypnotic.

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Alvodine is the first narcotic analgesic with action approaching "pure" analgesia. It relieves pain without producing sedation, drowsiness or drugged sensation.* This unique characteristic makes Alvodine the most desirable agent for pain relief in these three large groups of patients.

Alvodine Tablets, 50 mg., scored.
Alvodine ampuls, 1 cc. containing 20 mg. per cc.
Narcotic blank required.
Write for detailed information on clinical experience, addiction liability, side effects and precautions.

*In more than 90% of patients

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Case Reports

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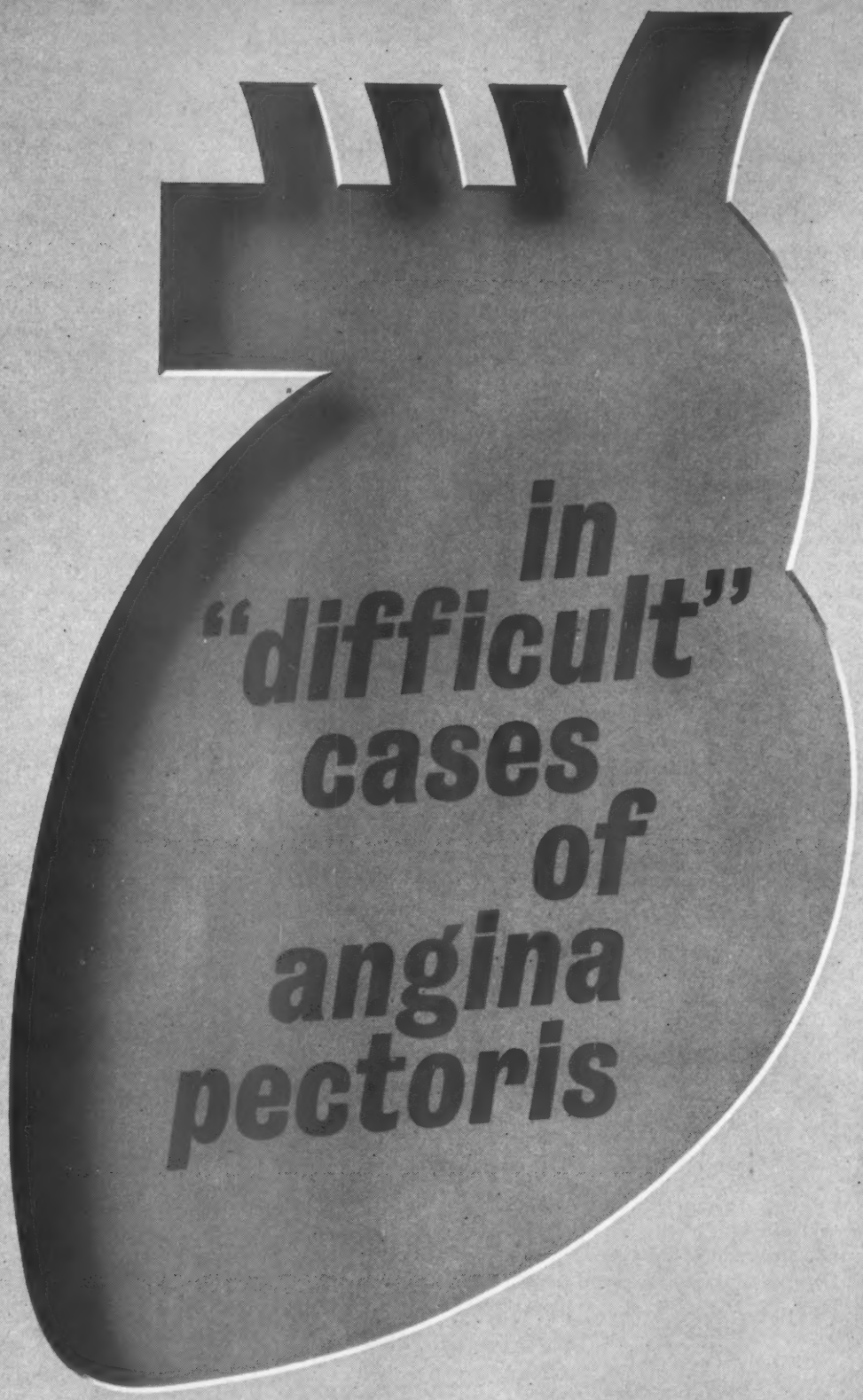

in "difficult" cases of angina pectoris

Marplan

prevents anginal pain[1-4]
increases exercise tolerance[2,5,6]
reduces nitroglycerin requirements[2,3]

A potent regulator of amine oxidase, Marplan has demonstrated a high degree of effectiveness in moderately severe to intractable angina pectoris. Improvement on Marplan ranged from a reduction in the number of attacks to virtual abolition of the anginal state. With Marplan, anginal relief is enhanced by a more confident mental climate — improving the chances of success of the entire prophylactic regimen. However, since the precise manner in which Marplan improves the cardiac status is as yet undefined, it is imperative that patients be instructed to maintain the same restrictions of activity in force prior to Marplan therapy. Consult literature and dosage information, available on request, before prescribing.

References: 1. W. Hollander and R. W. Wilkins, in J. H. Moyer, Ed., Hypertension, Philadelphia, W. B. Saunders Co., 1959, p. 399. 2. R. W. Obiath, paper read at American Therapeutic Society, 60th Annual Meeting, Atlantic City, N. J., June 6, 1959. 3. N. Bloom, **Virginia M. Month.**, 87:23, 1960. 4. T. Winsor and P. Zarco, **Angiology**, 11: (Part 2), 67, 1960. 5. G. C. Griffith, **Clin. Med.**, 6:1555, 1959. 6. G. C. Griffith, **Dis. Nerv. System**, 21 (Suppl.), 101, 1960.

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Special Departments

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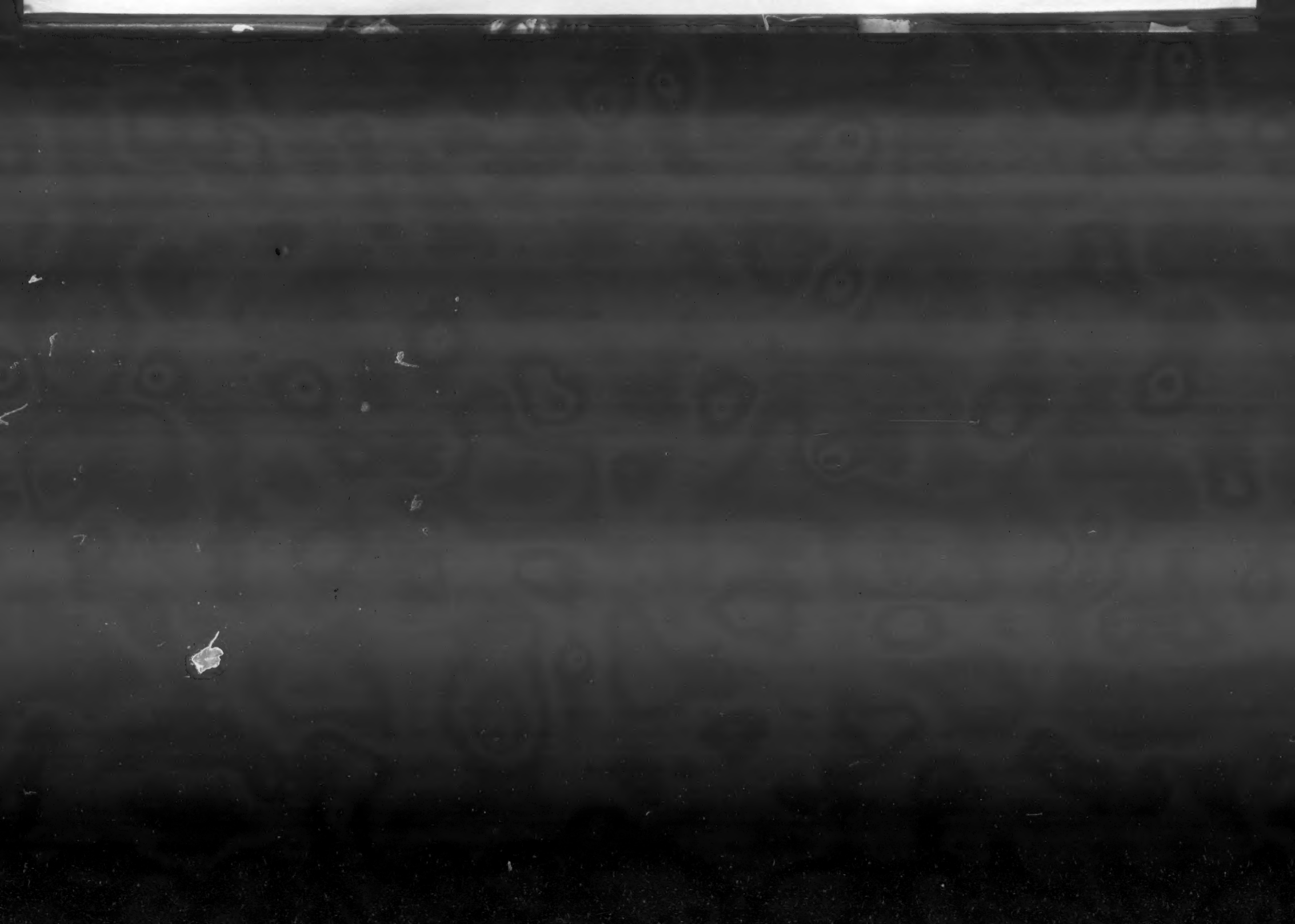
Now! 2 appetizing foods make serum cholesterol control easier, more effective than ever!



Your Patients Can Enjoy Fine Foods With Minimum Diet Changes!

For good eating while maintaining serum cholesterol control

Leading authorities agree that where reduction of serum cholesterol levels is indicated, fat intake should not exceed ⅓ of total calories and of this, at least ⅓ should be polyunsaturated fats.

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Mazola Margarine* contains *liquid* Mazola Corn Oil as a major ingredient. This corn oil is not hydrogenated, thereby preserving its rich content of linoleates. Mazola Margarine contains 2 to 3 times as much natural linoleates as any other margarine readily available in grocery stores from coast to coast. Its taste, color and handling characteristics are unexcelled.

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AVERAGE COMPOSITIONS OF MAZOLA® MARGARINE AND MAZOLA® CORN OIL
(All figures are in grams.)

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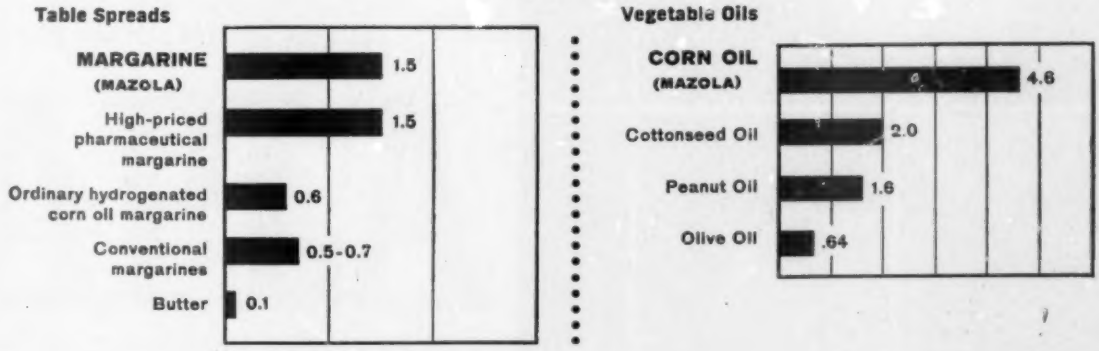
	100 grams	2 oz. (4 tbsp.)	100 grams	1 fl. oz. (2 tbsp.)
Fatty Acids				
Polyunsaturated	21	12	51	14
Monounsaturated	40	23	32	9
Saturated	14	8	11	3
Natural Sitosterols	0.5	0.3	1	0.3
Natural Tocopherols	0.08	0.045	0.08	0.020
Cholesterol	none	none	none	none
Sodium	0.9	0.5	none	none

MAZOLA MARGARINE—410 Calories/2 oz.; Iodine Value—96
MAZOLA CORN OIL—250 Calories/fl. oz.; Iodine Value—124

RATIO OF POLYUNSATURATES/SATURATES
(Average values.)



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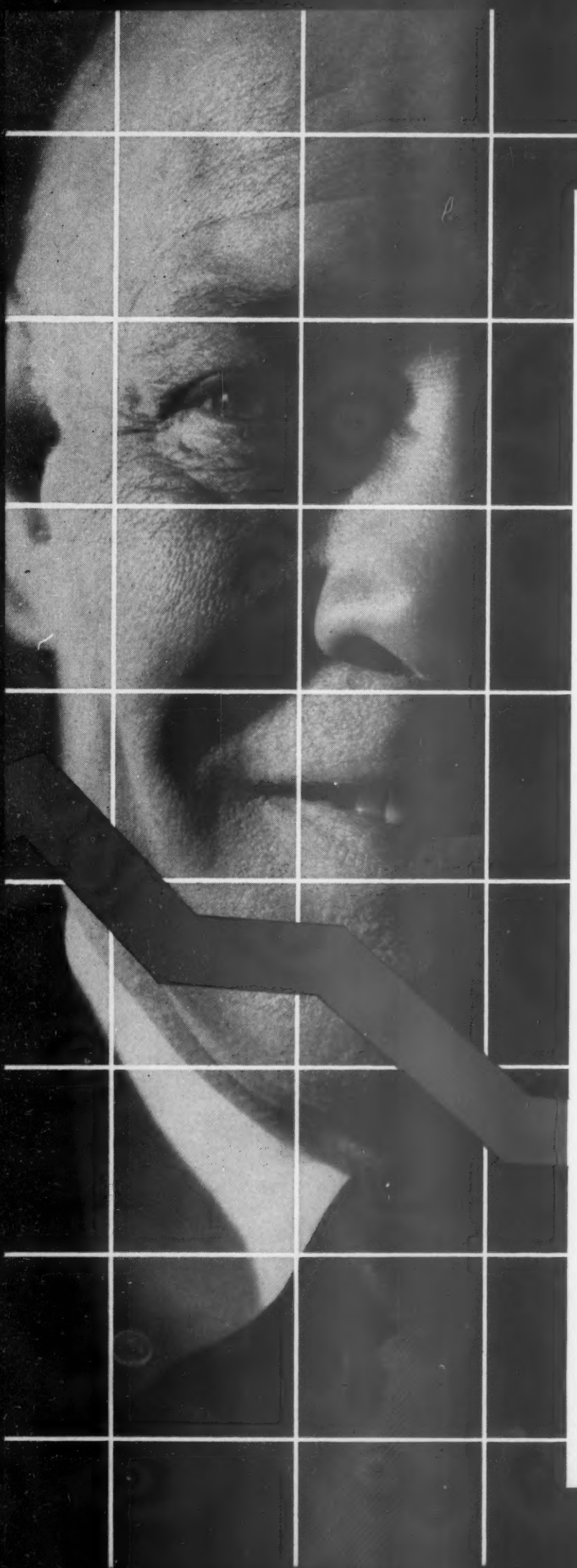

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A new drug to control without

Capla acts centrally

Capla reduces blood pressure by acting predominantly at the brainstem vasomotor center; is not a ganglionic blocker. It produces no depression, no postural hypotension, no nasal congestion, no gastric hyperacidity. Transient drowsiness sometimes occurs, usually at higher dosages. Capla has proved exceptionally well tolerated in clinical use and has no known contraindications.

New therapy

Alone, Capla is highly effective for mild to moderate hypertension. In more severe cases, it can be combined with diuretics or peripherally acting antihypertensives.

Mild calming effect

Patients on Capla often report a mild calming effect. This action, together with the unusual freedom from serious side effects, makes therapy with Capla gratifying for both the patient and the physician.

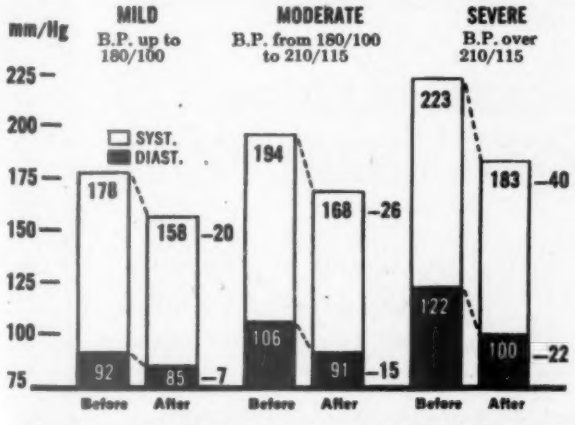
CAPLA™

that works in a new way blood pressure serious side effects

at the brainstem vasomotor center

Proved effective in clinical use

Average reductions in systolic and diastolic blood pressure reported with Capla (325 patients)



Usual dose. Capla 300 mg., q.i.d.—duration of therapy. 3 weeks to over 1 year.

The chart shows that Capla reduces both systolic and diastolic pressures, usually in proportion to pre-therapy levels.

Recommended Dosage: One 300 mg. tablet three or four times daily, before meals and at bedtime. The dosage should be adjusted to individual requirements; for example, older patients may require lower dosage.

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CLINICAL & PHARMACOLOGICAL REPORTS 1. Berger, F. M., and Margolin, S.: A Centrally Acting Blood Pressure Lowering Agent (W-583). Fed. Proc. *20:*113 (March) 1961. 2. Diamond, S., and Schwartz, M.: Scientific Exhibit at Ill. State Med. Soc. Chicago, (May) 1961. 3. Douglas, J. F., Ludwig, B. J., Ginsberg, T. and Berger, F. M.: Studies on W-583 Metabolism. Fed. Proc. *20:*113 (March) 1961. 4. Duarte, C., Brest, A. N., Kodama, R., Naso, F., and Moyer, J. H.: Observations on the Antihypertensive Effectiveness of a New Propanediol Dicarbamate (W-583). Curr. Ther. Res., *2:*148-52 (May) 1960. 5. DuChez, J. W., Scientific Exhibit at Amer. Academy of Gen. Practice, Miami, (April) 1961. 6. Kletzkin, M., and Berger, F. M.: A Centrally Acting Antipressor Agent, Fed. Proc. *20:*113 (March) 1961. 7. Mulinos, M. G., Scientific Exhibit at Amer. Coll. Card. New York, (May) 1961. 8. Mulinos, M. G., Saltefors, S., Boyd, L. J., and Cronk, G. A.: Human Pharmacology Studies with W-583. Fed. Proc. *20:*113 (March) 1961. 9. Shubin, H., Scientific Exhibit, Amer. Coll. Card. New York (May) 1961.

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FIRST PRIZE IS REPRESENTED BY A SILVER MEDAL AND $1,000.

Honorable Mention $250; Eight Additional Awards of $100 Each.

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SCOPE A formal presentation, 10 minutes in length, describing original investigation in which the contestant did either the work or was a significant member of investigating team.

PROCEDURE An original manuscript and letter indicating intention to enter the competition must be in hands of Executive Director by *January 1, 1962.*

An *accompanying* letter from the chief of the service or laboratory indicating his willingness to have the material presented in the competition.

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Competition to be in Denver, Colorado, upon the occasion of the 11th Annual Meeting of the American College of Cardiology, date May 29 to June 2, 1962.

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This is why Miltrate gives better protection for the heart than vasodilators alone in coronary insufficiency, angina pectoris and postmyocardial infarction.

Miltrate contains PETN (pentaerythritol tetranitrate), acknowledged as basic therapy for long-acting vasodilation. . . .

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REFERENCES: 1. Ellis, L. B. *et al.:* Circulation *17*:945, May 1958. 2. Friedlander, H. S.: Am. J. Cardiol. *1*:395, Mar. 1958. 3. Riseman, J.E.F.: New England J. Med. *261*:1017, Nov. 12, 1959. 4. Russek, H. I. *et al.:* Circulation *12*:169, Aug. 1955. 5. Russek, H. I.: Am. J. Cardiol. *3*:547, April 1959. 6. Tortora, A. R.: Delaware M. J. *30*:298, Oct. 1958. 7. Waldman, S. and Pelner, L.: Am. Pract. & Digest Treat. *8*:1075, July 1957.

Supplied: Bottles of 50 tablets. Each tablet contains 200 mg. Miltown and 10 mg. pentaerythritol tetranitrate.

Dosage: 1 or 2 tablets q.i.d. *before meals* and at bedtime, according to individual requirements.

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Miltown® (meprobamate)+PETN

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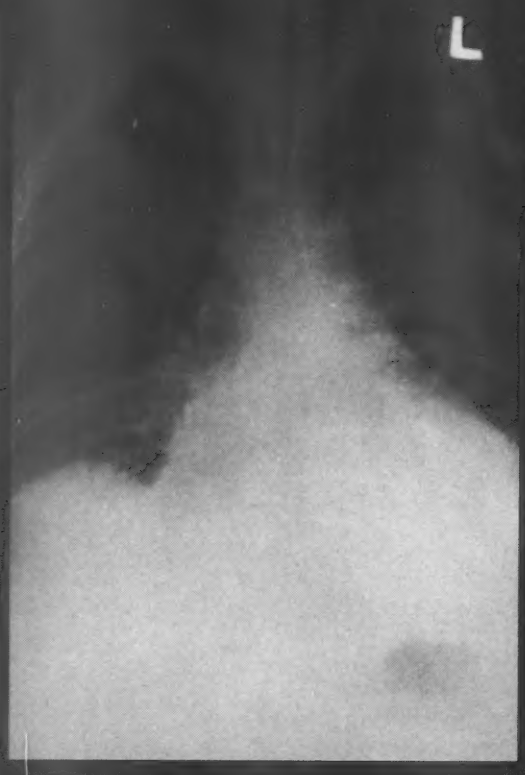
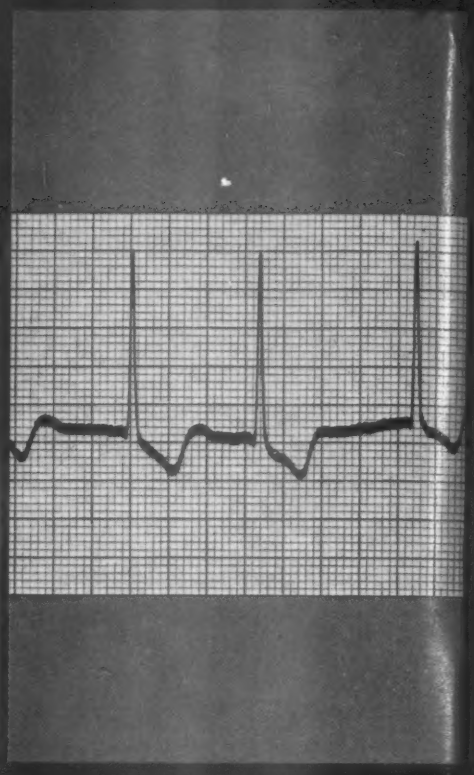
*before treatment**

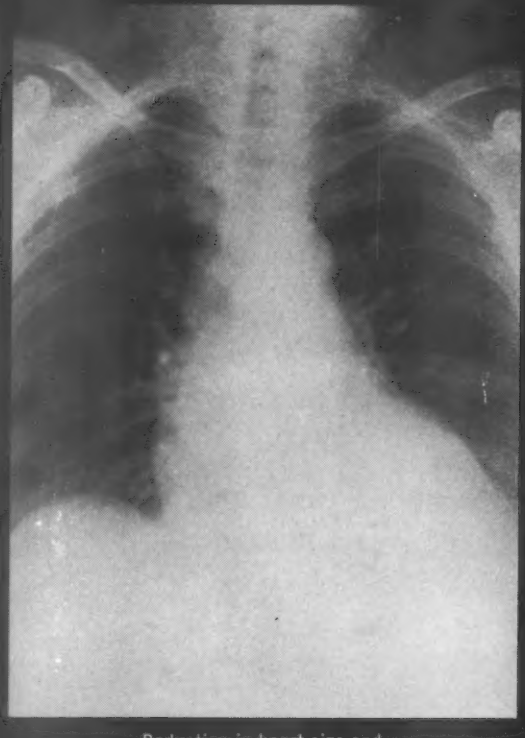


Cardiac enlargement and pulmonary congestion.

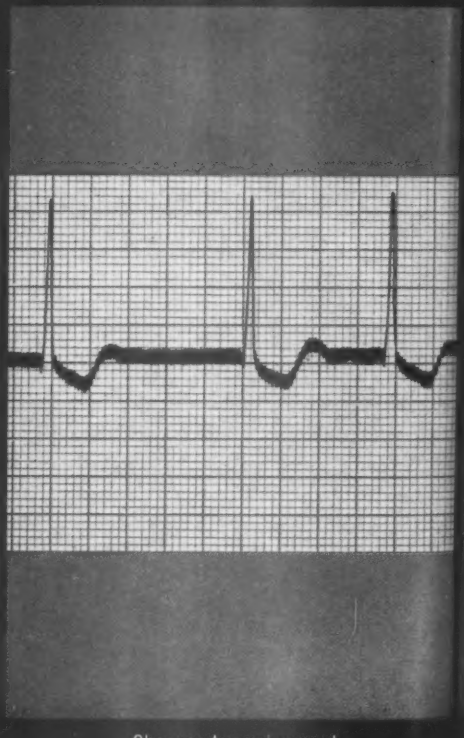


Left ventricular strain and hypertrophy (ST depression in Lead V4).

after one month on HYDROPRES*



Reduction in heart size and clearing of congestion.



Changes toward normal (less ST depression).

*case report

effective by itself in many hypertensives...
indicated in all degrees of hypertension

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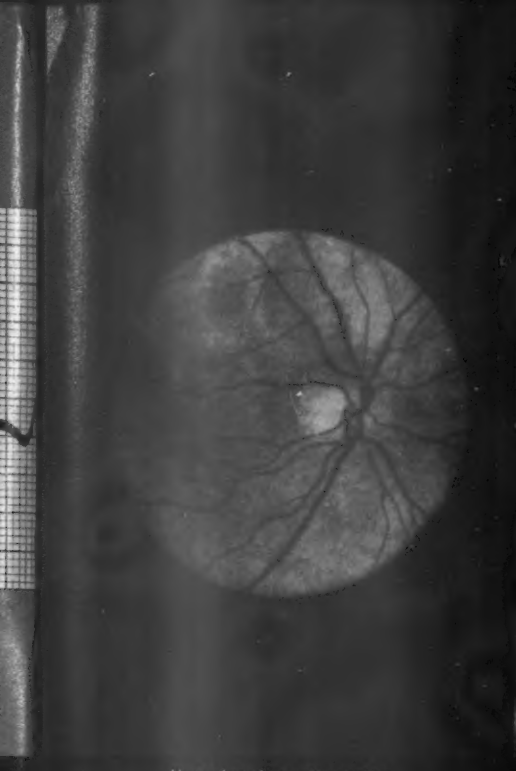
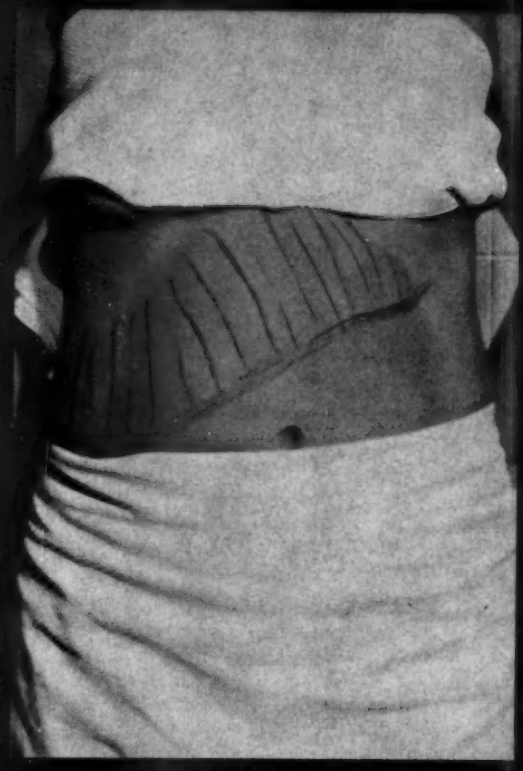
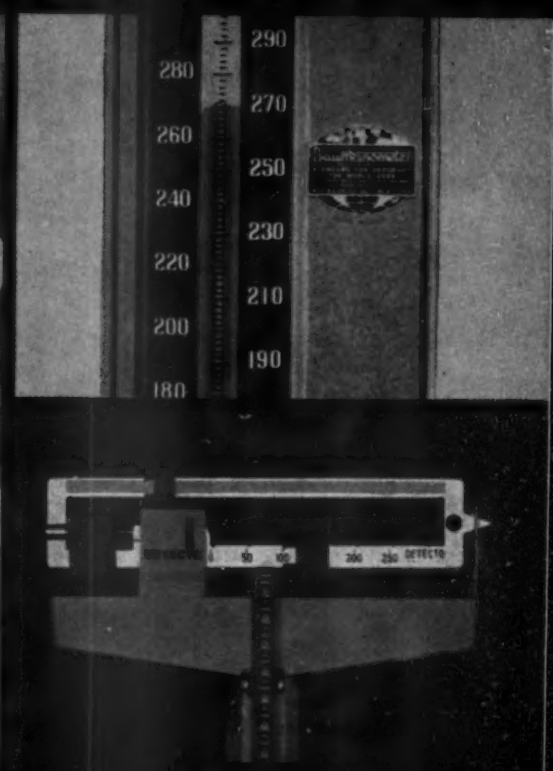
HYDRODIURIL® with RESERPINE
HYDROCHLOROTHIAZIDE



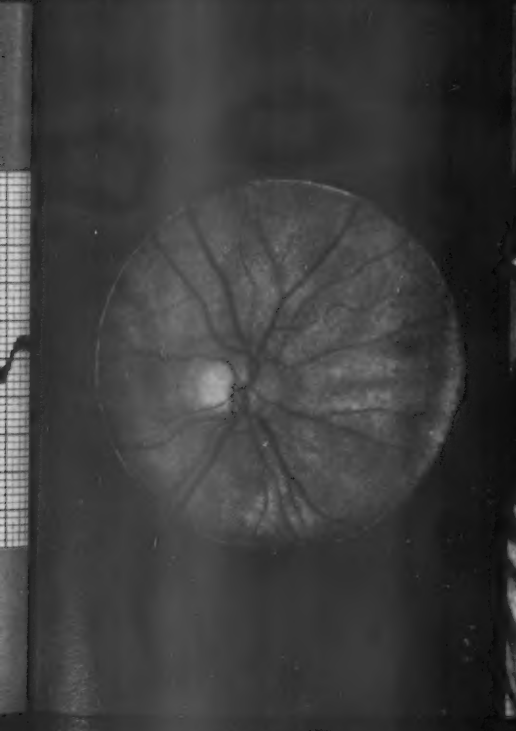
Hypertensive retinopathy with hemorrhages.



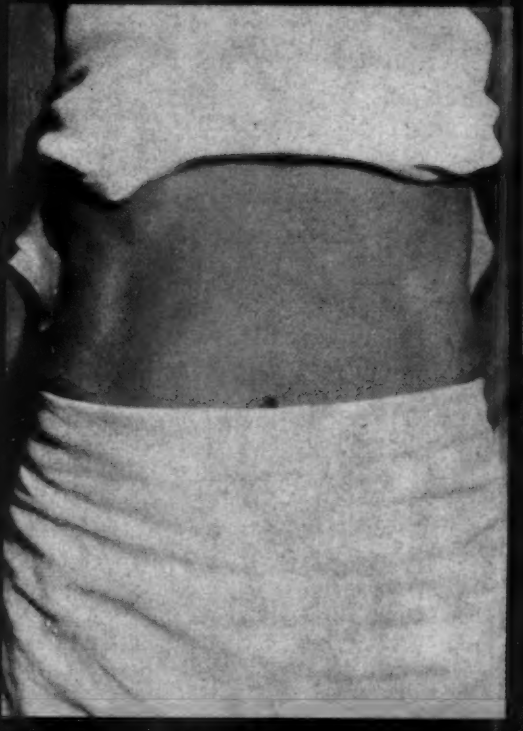
Liver palpable 5 fingerbreadths below costal margin.



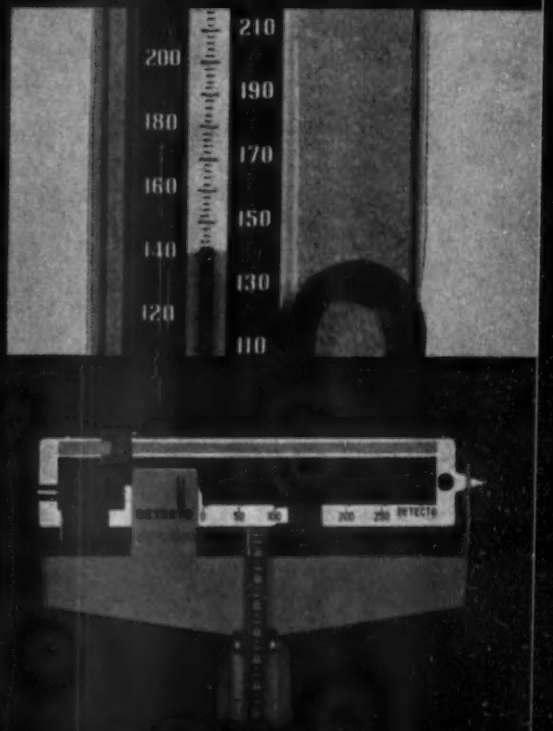
Blood pressure 270/120.
Weight 110½ pounds.



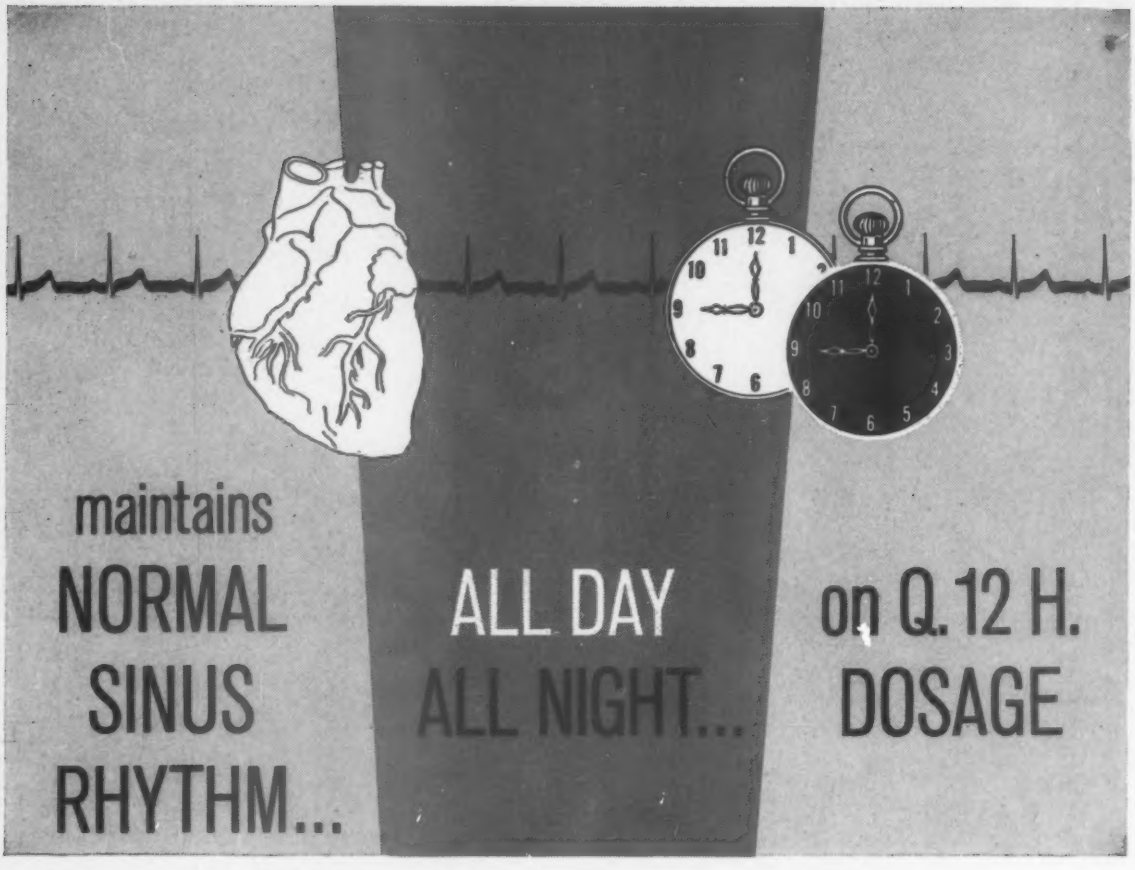
Very little change.



Liver not palpable.



Blood pressure 140/72.
Weight 105 pounds.



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Quinidine Gluconate 5 gr. (0.33 Gm.)

IN CARDIAC ARRHYTHMIAS[1-10]

Maximum efficacy: maintains effective quinidine blood levels all day, all night. **Better tolerated:** because quinidine gluconate is 10 times as soluble as the sulfate, and only part of daily Dura-Tab dosage contacts gastric mucosa. **Maximum convenience:** given q. 12 h.—no night dosage needed.

DOSAGE: for conversion of auricular fibrillation to normal sinus rhythm, in most cases, 2 Dura-Tabs 3 or 4 times a day, for 2 to 3 days; longer periods are required in some patients. **For maintenance,** 2 Dura-Tabs q. 12 h. in most patients . . . Bottles of 30, 100 and 250 Quinaglute Dura-Tabs.

For SAMPLES and complete literature[1-10] giving indications, cautions, etc., write

REFER TO PDR Page 821

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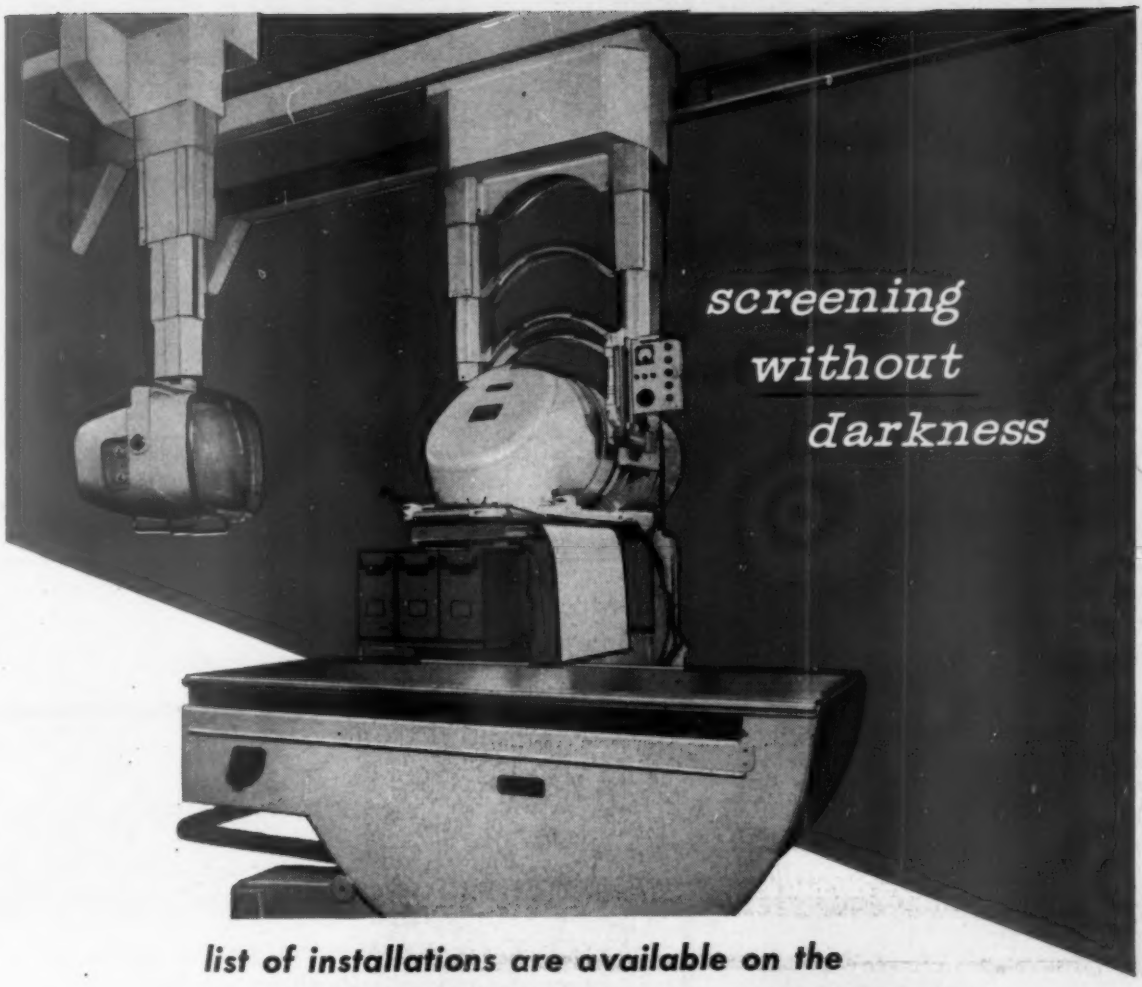
*U.S. Patent 2,895,881

also available INJECTABLE QUINAGLUTE



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after 3 years' clinical experience:
here is what we now know about MER/29 and .

WE KNOW HOW MER/29 ACTS

We know that MER/29 lowers cholesterol in 8 out of 10 patients, even without dietary restrictions. In 576 patients studied by various physicians, average cholesterol levels dropped from 303 mg. % to 241 mg. % —an average decrease of 62 mg. %.

We know that MER/29 reduces total sterols in both blood and tissue.

We know that MER/29 does this by inhibiting the body's own production of cholesterol.

We know that its use in over 300,000 patients reaffirms the safety margins established in early laboratory and clinical data.

OTHER MEASURES No other measures are proven to reduce tissue cholesterol even in the face of serum cholesterol reduction.

MER/29 Studies in patients have demonstrated a reduction of approximately 40% of tissue cholesterol, as well as a significant reduction of the total sterol pool.

effect on
body pool of cholesterol

WE KNOW THE BENEFITS OF MER/29

We know that, in some patients, concurrent clinical benefits attend the use of MER/29. Published papers on MER/29 therapy to date report improvement in 50 of the 79 anginal patients reported in these studies, and comparable results are being obtained in similar studies now in progress. Among the other benefits reported are:

decreased incidence and severity of anginal attacks

improved* ECG *patterns

diminished nitroglycerin dependence

increased sense of well-being

"During triparanol [MER/29] therapy there was a definite improvement in the electrocardiographic tracings in response to exercise in 3 of 11 subjects with angina pectoris." —*Hollander, W.*, et al.: *J.A.M.A.* 174:*5 (Sept. 3) 1960.*

"Nitroglycerine requirements decreased in 3 [of 5 outpatient] patients, including the patient showing electrocardiographic improvement....Three [of 4 private male patients], after a lapse of some weeks, showed improvement in exercise electrocardiograms, which was sustained but not further improved in subsequent observations." —*Corcoran, A. C.*, et al.: *Progr. Cardiovasc. Dis.* 2: *(Pt.1) 576 (May) 1960.*

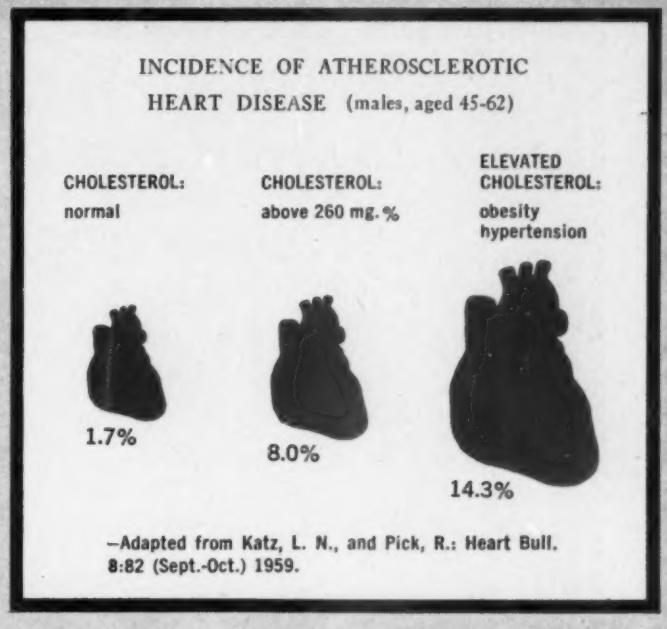
"Of the 45 patients with coronary artery disease followed for 1 year, 16 had a history of frequent anginal attacks. Fourteen of these spontaneously stated that their angina disappeared within 2 months of [MER/29] therapy....In one patient...with persistent coronary insufficiency pattern (ST segment depressions in multiple leads), there was a complete reversion to a normal tracing during MER/29 therapy with associated clinical improvement in angina." —*Lisan, P.: Progr. Cardiovasc. Dis.* 2: *(Pt. 1) 618 (May) 1960.*

d . . . . what we are learning about atherosclerosis

[redacted]

"It has become generally accepted that elevated blood cholesterol or lipid, if sustained long enough, leads to early atherosclerosis."
–Page, I. H.: Mod. Med. 29:71 (Mar. 20) 1961.

Epidemiologic studies show that low cholesterol levels are associated with low incidence of atherosclerosis and coronary artery disease. On the basis of such studies, Stamler has said: "...a 15 to 20 per cent reduction in mean serum cholesterol levels alone might be associated with a 25 to 50 per cent reduction in coronary disease incidence rates in middle-aged men."
–Stamler, J.: Am. J. Pub. Health 50:(Pt. 2) 14 (Mar.) 1960.



[redacted]

Despite our knowledge of the action, benefits and safety of MER/29, much remains to be discovered about the basic concept of cholesterol-lowering therapy. In this, MER/29 is comparable to the well-accepted use of antihypertensive agents: we know they lower blood pressure, but we cannot prove that lowering blood pressure will also lower morbidity or mortality. Yet few physicians hesitate to use these agents. The possible good is too great to ignore.

So it is with MER/29. No one can yet be certain that sustained, effective lowering of total body sterols will prevent or alter atherosclerosis. But the current evidence strongly supports this concept.

Perhaps that's why a growing number of physicians are now prescribing MER/29. They wish to assure their hypercholesterolemic, coronary artery disease, and atherosclerotic patients this reasonable hope.

It is a decision facing every physician.

Complete bibliography and prescription information on request.

Still available... write for your copy of this full-length report.

MER/29
(triparanol)

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Division of Richardson-Merrell Inc.
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A 30 mg. Pentritol Tempule containing hundreds of pellets for 12 hour action produces a smooth, prolonged response similar to modern depot injections. Duration, frequency, and severity of anginal attacks are lessened.[1] Patients showing little progress with 80 mg. daily of PETN tablets, respond favorably to the smaller dose of Pentritol Tempules.[2] Kamil and Klinger report excellent results from a timed-disintegration pentaerythritol tetranitrate capsule, with nitroglycerin requirements reduced as much as 85%.[3]

PENTRITOL® TEMPULES

controlled disintegration capsules

1. Biegeleisen, H. I.: Clin. Med. *2*:1005, 1955. 2. Roberts, J. T.: Clin. Med. *4*:1375, 1957. 3. Kamil, M., and Klinger, I.: New York State J. Med. *59*:3398, 1959.

PENTRITOL—Each Pentritol Tempule is a controlled disintegration capsule containing 30 mg. of pentaerythritol tetranitrate in granular form. An initial dose of 10 mg. is released at once; a second dose 4 hours later; and a third dose 8 hours after ingestion. Thus, each Tempule affords at least 12 hours of coronary vasodilation. ACTION AND USES: Effective therapy for and prophylaxis against anginal attacks. One Tempule morning and evening will provide 24 hours of effective medication, with a smooth, sustained clinical effect that has shown superior results. Pentritol reduces or eliminates nitroglycerin requirements, stops or reduces frequency of anginal attacks, eliminates or mitigates pain, and increases capacity for physical activity. CONTRAINDICATIONS: Observe caution in glaucoma. DOSAGE: One Pentritol Tempule morning and evening, approximately 12 hours apart. SUPPLIED: Bottles of 60 and 250. Also available: Pentritol®-B Tempules®, with 30 mg. pentaerythritol tetranitrate and 50 mg. butabarbital, for 12 hours of coronary vasodilation plus sedation.

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CLINICAL OPINION

"...the magnitude of the response to 15 mg. ['Cardilate'] was comparable to that following nitroglycerin....The comparatively prolonged duration of action of erythrol tetranitrate when given sublingually makes it especially valuable for clinical use."[1]

CLINICAL OPINION

"Nitroglycerin and erythrol tetranitrate when administered sublingually are among the most potent of all prophylactic agents available for the treatment of patients with angina pectoris."[2]

CLINICAL OPINION

"Erythrol tetranitrate exhibits an inherent long-acting vasodilating effect. Therefore it is the drug of choice in angina pectoris."[3]

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Erythrol Tetranitrate Sublingual Tablets

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5 mg., scored 

15 mg., scored 

Bottles of 100 tablets.

Complete literature available on request.

1. Riseman, J.E.F., *et al.*: Circulation *17*:22 (Jan.) 1958.

2. Russek, H.I.: Circulation *18*:774 (Oct.) 1958.

3. Hirshleifer, I., *et al.*: Scientific Exhibit, A.M.A., Atlantic City, N. J., June, 1959.

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5-year study[1] with COUMADIN demonstrates: long-term anticoagulation in office management of outpatients is practical and effective

A 5-year study[1] of long-term anticoagulation with COUMADIN (warfarin sodium) in office practice patients has demonstrated that such treatment reduces the probability of further infarctions in the postinfarct patient and is effective in preventing a first infarction in patients with angina.

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1. Nora, J. J.: M. Times, May, 1961. 2. Nora, J. J.: J.A.M.A. 174:118, Sept. 10, 1960. 3. Baer, S., et al.: J.A.M.A. 167:704, June 7, 1958. 4. Moser, K. M.: Disease-a-Month, Chicago, Yr. Bk. Pub., Mar., 1960, p. 13. 5. Meyer, O. O.: Postgrad. Med. 24:110, Aug., 1958.

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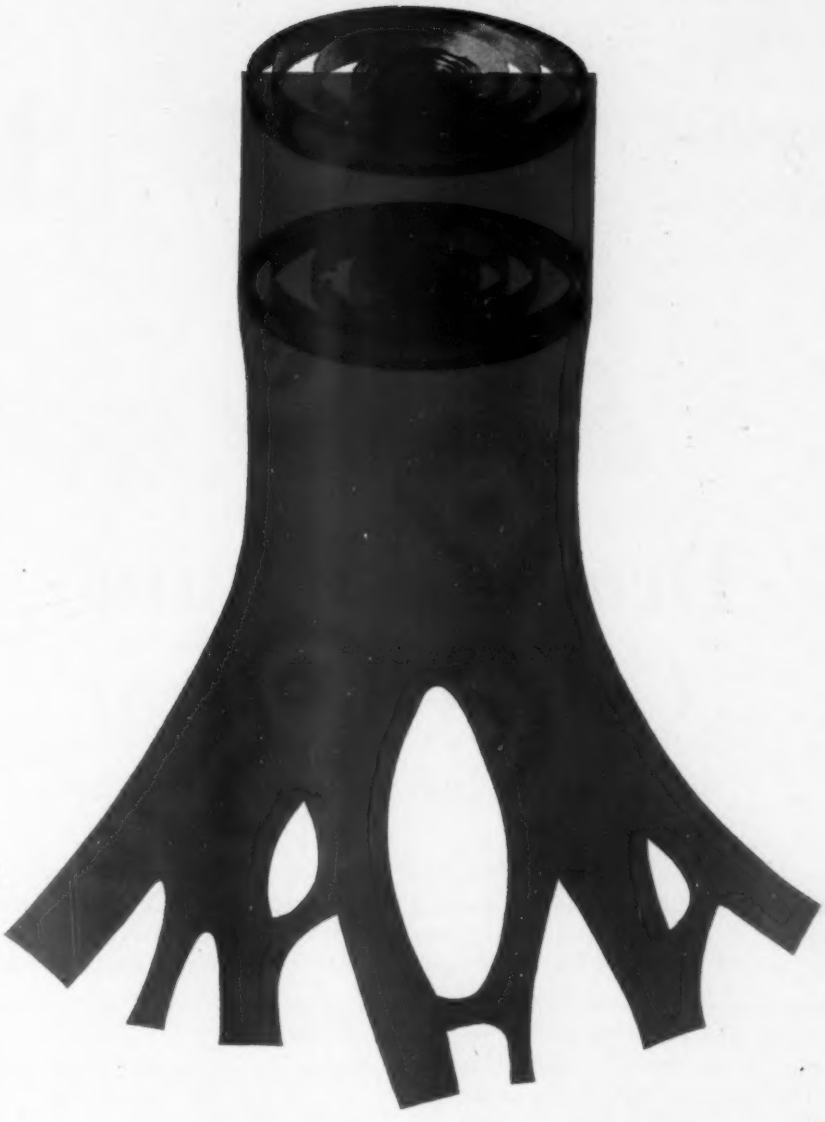

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References: 1. Ford, R. V.: Current Therap. Research 2:347, 1960. 2. Fuchs, M., and others: Current Therap. Research 2:11, 1960. 3. Ford, R. V.: Connecticut Med. 24:704-707, (Nov.) 1960. 4. Ford, R. V.: Texas State J. Med. 56:343, 1960.

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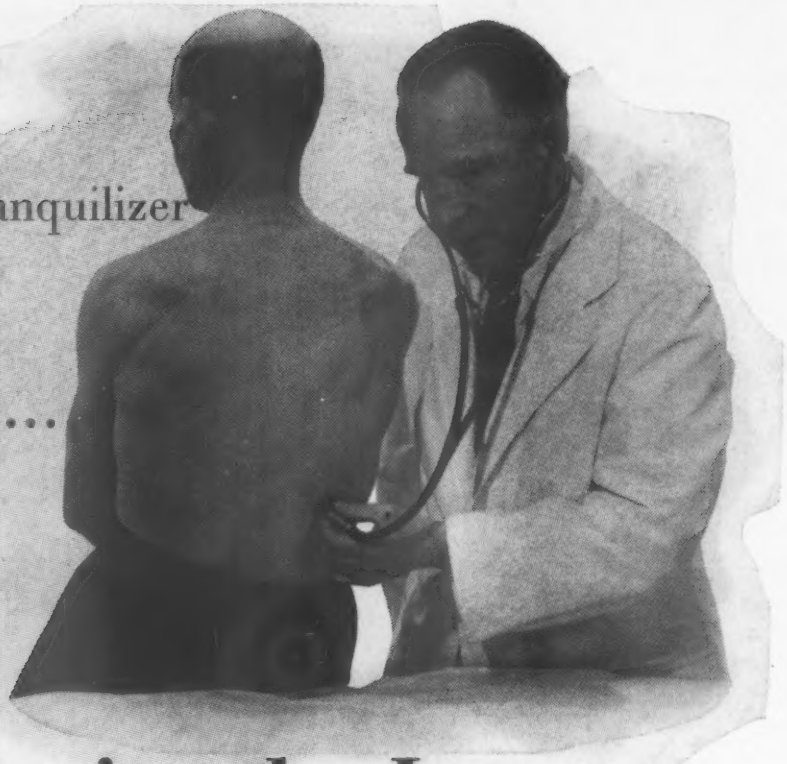

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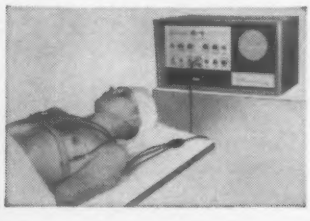

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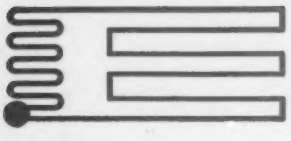

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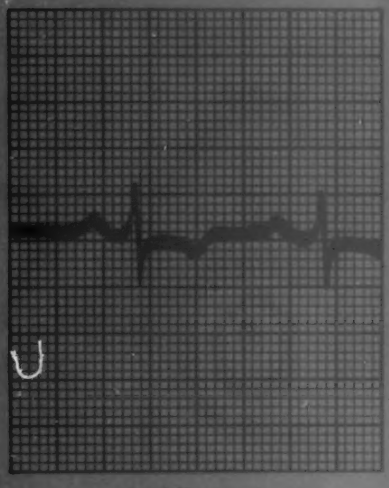
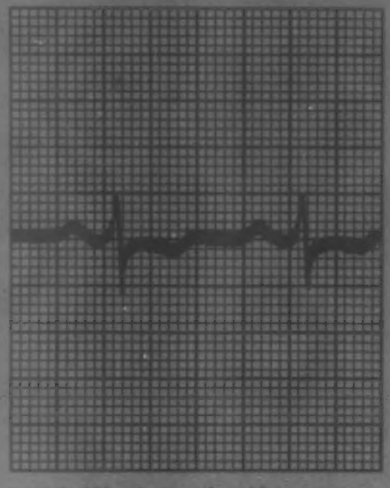
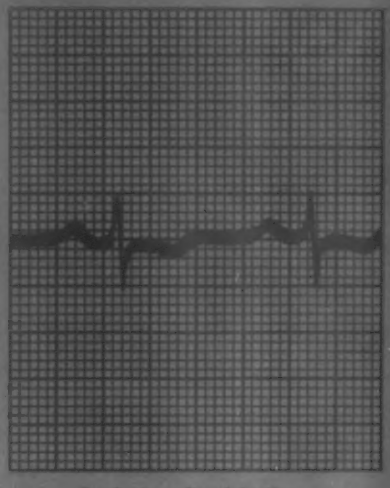


Lead II: at rest.



Lead II: 1½ minutes after 10 mg. TENUATE i.v.—equivalent to 100 mg. oral dose (4 times the recommended oral dose).



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TENUATE suppresses appetite with unique advantages for "special risk" patients: no effect on heart rate, blood pressure, pulse or respiration,[1] no alteration of BMR.[2]

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References: 1. Alfaro, R.D., Gracanin, V. and Schlueter, E.: J. Lancet 80:526, 1960. 2. Huels, G.: Michigan Acad. Gen. Pract. Symposium, Detroit, 1959. 3. Horwitz, S.: Personal communication, 1959. 4. Spielman, A.D.: Michigan Acad. Gen. Pract. Symposium, Detroit, 1959. 5. Ravetz, E.: Michigan Acad. Gen. Pract. Symposium, Detroit, 1959. 6. Declna, L.J.: Exper. Med. & Surg. *(in press)*. 7. Scanlan, J.S.: Personal communication, 1959. 8. Kroetz and Storck: Personal communication, 1959.

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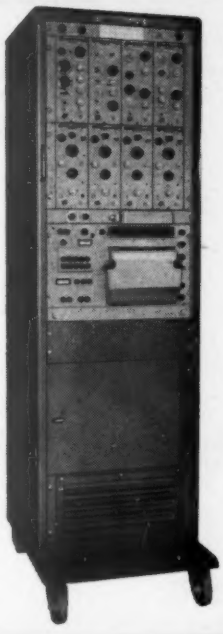

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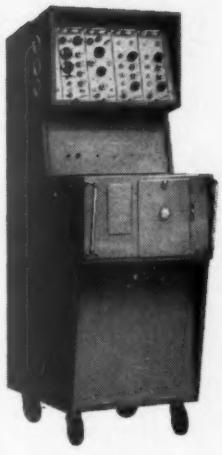

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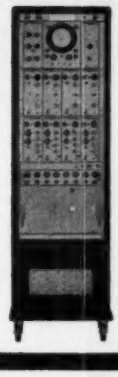

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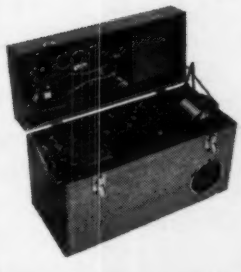
Versatile Poly-Beam system uses up to eight "350" preamplifiers; excellent performance, full-scale (15 cm) recording, reproducible traces; monitor units may be included.

2-Channel Photographic Model 62 Twin-Beam



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The American Journal of Cardiology

VOLUME VIII AUGUST 1961 NUMBER 2

Clinical Studies

Comparison of the Amount of Coronary Arteriosclerosis in Autopsied East Africans and New Yorkers*

R. FOSTER SCOTT, M.D., A. S. DAOUD, M.D., R. A. FLORENTIN, M.D.

Albany, New York

J. N. P. DAVIES, M.D. (Bristol), M.R.C.S., L.R.C.P. *and* RUTH M. COLES, B.SC.

Kampala, Uganda

THIS STUDY is one of a series[1-6] designed to explore the possible interrelationships in man and animals of coronary arteriosclerosis, thrombosis, myocardial infarction and lipid patterns in blood and tissue. This report deals specifically with a direct comparison of the amount of coronary arteriosclerosis and incidence of myocardial infarcts in autopsied subjects from two geographic areas: Uganda, East Africa, and upper New York State.

Studies, both clinical and anatomic, have been made of the degree of arteriosclerosis and incidence of myocardial infarcts in the Negro of South Africa. Autopsy studies indicate that this group is not free of arteriosclerosis, although no significant amount is present in younger subjects. Over the age of thirty-four years one-half of the South African Negro group studied by Laurie, Woods and Roach[7] showed coronary arteriosclerosis to some degree, but had only a 1.4 per cent incidence of frank myocardial infarction. No comparisons by the same observers of the severity of anatomic arteriosclerosis and number of myocardial infarcts in hearts of South African Negroes compared directly to hearts of Americans appear to have been done, however. Values of serum cholesterol in South African Negroes over forty years of age have been found to be low as compared to American values for the same age group.[8]

Studies of East Africans of Uganda indicate that they have low serum cholesterol levels, with a mean of 150 mg. per cent.[9] The incidence of myocardial infarction and of venous thrombi and pulmonary thromboembolic phenomena has been reported to be exceedingly low among East Africans, even in older age groups,[4] as compared with the established high incidence among North Americans.[10] However, no quantitative studies of the comparative amount of coronary arteriosclerosis and number of myocardial infarcts in East Africans and Americans have been made with direct comparisons by the same observers. Before starting elaborate chemical and clot lysis studies related to the degree of arteriosclerosis in these groups, it seemed essential to make such direct comparisons by quantitative methods. Therefore,

* From the Departments of Pathology, Albany Medical College, Albany, New York and Makerere College, University College of East Africa, Kampala, Uganda. This study was supported by PHS Grants H-4727, H-4791 and H-4130, National Institutes of Health, Bethesda, Maryland.

TABLE I

Age and Sex Distribution of 117 Autopsied Subjects over Sixteen Years of Age at Mulago Hospital, Kampala, Uganda and 137 from Albany Hospital, Albany, New York

Age (yrs.)	New York Autopsy Series		East African Autopsy Series	
	Men	Women	Men	Women
16–29	1	2	20	11
30–39	1	3	23	6
40–49	10	7	20	2
50–59	10	11	11	1
60–69	19	15	9	4
70–79	25	15	5	2
80–89	10	8	1	1
90–99	0	0	1	0

hearts from 117 East African Negroes were sent to Albany, New York, and compared with 137 hearts from autopsied white New Yorkers.

MATERIALS AND METHODS

East African Autopsy Series: Material and data from 117 autopsies performed by the staff of the Department of Pathology, Makerere Medical College, and Mulago Hospital in the spring and summer of 1960 were used in this study. Mulago is a 700 bed general hospital admitting only African patients (no Europeans or Indians) and is located in Kampala, Uganda. The series was consecutive for all autopsies on subjects sixteen years of age and over except for four cases of endomyocardial fibrosis, three cases of metastatic carcinoma of the myocardium, three of rheumatic fever, and twenty-two cases either used for teaching purposes or inadvertently discarded. Medicolegal autopsies performed by pathologists other than those in the Department of Pathology were not included in the series. None were excluded for any reason related to arteriosclerosis. All hearts from East Africa were fixed in a 10 per cent formalin for at least two weeks and sent to Albany where they were examined and measured as will be described. The age and sex distribution of the series is shown in Table I.

New York Autopsy Series: One hundred thirty-seven autopsied subjects sixteen years of age and over from Albany Medical Center Hospital were included in this study. The autopsies were performed by the resident staff of the Department of Pathology, Albany Medical College, under the supervision of senior members of the department. The period of time from which the autopsies were selected was roughly comparable to that for the East African series. The cases were consecutive except that seven hearts were taken for radiographic studies of the coronary arterial tree, seven were excluded because of infectious disease such as hepatitis or tuberculosis, eight were excluded because of incomplete autopsy data and eight were inadvertently destroyed. All Negroes were excluded from the series. The age and sex distribution of the cases is shown in Table I.

Matching of Cases: In order to make more meaningful comparisons of coronary arteriosclerosis in the two autopsy series, as many subjects as possible forty years of age and over from each series were matched for age and sex. The matching was done as follows: all autopsies on subjects over forty years in each group were ranked according to autopsy number. The first man from the African series was then matched with the first man in the American series whose age was identical; if no identical age-match could be made, the autopsy from the American series having the closest age within one, two, or three years of the African autopsy was matched. If no match within a three year age span could be made, the African autopsy was discarded from the age and sex-matched series. The second ranked African over forty years was matched similarly and so on. Women over forty years from the African series were matched with women over forty in the American series in the same manner.

Method of Examination of Hearts and Coronary Arteries: The hearts were examined systematically both grossly and microscopically for infarcts or other abnormalities. After fixation in 10 per cent formalin, the amount and severity of coronary arteriosclerosis were measured, using a method previously described by us in detail.[11] This method is based on the premise that, in general, the wall of a coronary artery thickens when it is involved by arteriosclerosis and that, in general, the degree and extent of thickening provides a reasonably good estimate of the amount of arteriosclerosis.

In brief, the procedure for the examination of the coronary arteries consists of a series of cross-sectional cuts along the course of the four main vessels (left, left descending, left circumflex and right coronary arteries). These right-angled cuts are made at accurately determined (with a special marking knife, Fig. 1) 5 mm. intervals until an external diameter of less than 1 mm. is reached. Alternate 5 mm. segments of vessel are then removed and the wall thickness determined (with specially designed calipers, Fig. 1) in two places on the proximal cut surface of the segment on a plane parallel to the epicardial surface. After measurement, these segments and the segments remaining on the heart are cut in thirds and examined minutely for occlusions, atheromatous plaques or hemorrhage into the wall. The entire procedure is designed to insure thorough and consistent examination of the major portions of the coronary arterial tree.

The chrome-plated steel calipers, made specifically for this purpose, are composed of two separately movable jaws and a post held in position between the jaws. The post is removable but once in position,

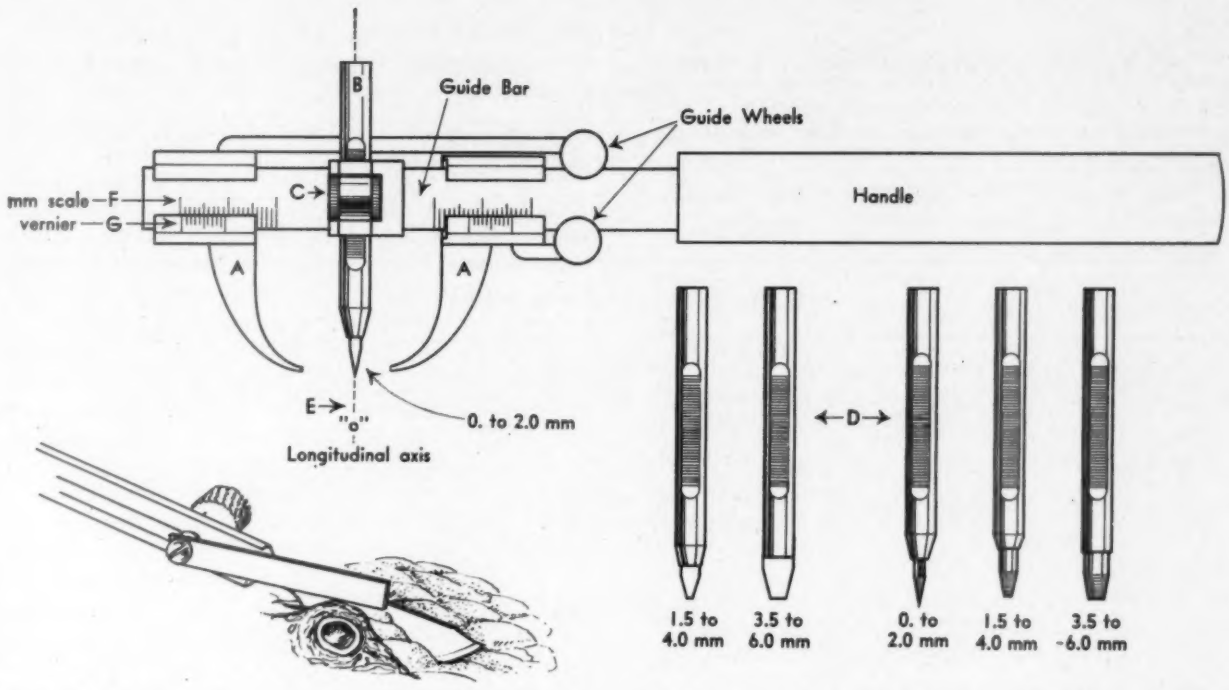

FIG. 1. Schematic drawing of specially designed calipers for the measurement of coronary wall thickness. Jaws (A), post in position (B), thumb screw for moving post (C), the longitudinal axis of the post representing the zero mark of the caliper scale (E), the millimeter scale (F) and the vernier (G). Shown separately are the interchangeable posts (D) of different sizes and shapes for various types of lumens, and the marking knife with its movable guide fixed 5 mm. from the blade.

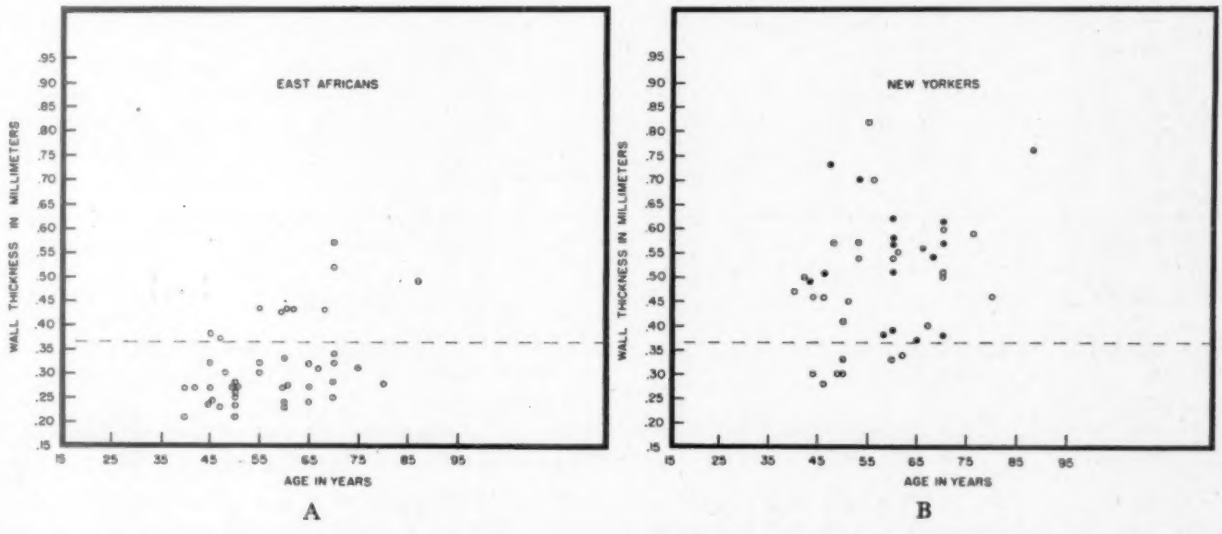

FIG. 2. The two scattergrams show the average coronary wall thickness in forty-three autopsied East Africans (A) and forty-three New Yorkers (B) over forty years of age matched for age and sex (thirty-four men and nine women in each group). Those with myocardial infarcts are indicated by ●. The line is drawn to indicate the least wall thickness with a myocardial infarct. It is apparent that most of the East Africans have values below this line but there is some overlapping.

can be moved only vertically, not horizontally. The longitudinal axis is at the 0 mark of the caliper scale. The guide bar on which the jaws travel is etched on each side of the post with a millimeter scale. The jaws are equipped with vernier scales, giving final readings to tenths of a millimeter.

Two sets of posts have been found necessary, with the tips of one set being flattened triangles for use in irregular lumens and the other set having rounded tips to use in a circular lumen. Each set contains three posts, with tapered tips accurately calibrated at 0 to 2 mm., 1.5 to 4 mm., and 3.5 to 6 mm. in diameter.

TABLE II

Mean Coronary Artery Wall Thickness for Each of the 117 Autopsied East Africans and 137 Autopsied New Yorkers*

Age (yr.)	Wall Thickness (mm.)	
	Men	Women
	A. East African Autopsy Series	
16–29	0.19, 0.21, 0.19, 0.22, 0.27, 0.27, 0.24, 0.33, 0.20, 0.26, 0.28, 0.20, 0.20, 0.21, 0.25, 0.26, 0.31, 0.23, 0.22, 0.25, 0.24	0.40, 0.25, 0.26, 0.29, 0.20, 0.22, 0.22, 0.21, 0.23, 0.23, 0.25
30–39	0.27, 0.25, 0.23, 0.26, 0.27, 0.25, 0.24, 0.25, 0.31, 0.25, 0.20, 0.27, 0.23, 0.29, 0.25, 0.27, 0.24, 0.25, 0.23, 0.31, 0.25, 0.35, 0.30	0.33, 0.24, 0.22, 0.23, 0.32, 0.28
40–49	0.24, 0.27, 0.27, 0.24, 0.38, 0.23, 0.30, 0.32, 0.37, 0.21, 0.31, 0.23, 0.23, 0.29, 0.26, 0.24, 0.40, 0.34, 0.30, 0.30	0.26, 0.27
50–59	0.26, 0.25, 0.43, 0.27, 0.21, 0.27, 0.28, 0.32, 0.30, 0.36, 0.39	0.23
60–69	0.27, 0.33, 0.24, 0.27, 0.31, 0.43, 0.43, 0.27, 0.23	0.43, 0.43, 0.32, 0.24
70–79	0.25, 0.28, 0.57, 0.52, 0.31	0.34, 0.32
80–89	0.49	0.29
90–99	0.34	
	B. New York Autopsy Series	
16–29	0.56	0.27, 0.62
30–39	0.40	0.40, 0.45, 0.38
40–49	0.73, 0.46, 0.30, 0.51, 0.47, 0.50, 0.57, 0.49, 0.28, 0.46	0.36, 0.27, 0.33, 0.25, 0.32, 0.46, 0.30
50–59	0.82, 0.38, 0.59, 0.30, 0.70, 0.45, 0.41, 0.54, 0.70, 0.57	0.56, 0.36, 0.31, 0.34, 0.41, 0.43, 0.36 0.40, 0.24, 0.33, 0.34
60–69	0.46, 0.57, 0.49, 0.54, 0.49, 0.62, 0.51, 0.61, 0.66, 0.54, 0.58, 0.40, 0.33, 0.46, 0.56, 0.57, 0.45, 0.39, 0.44	0.34, 0.46, 0.37, 0.61, 0.48, 0.46, 0.30, 0.66 0.33, 0.69, 0.39, 0.54, 0.56, 0.48, 0.62
70–79	0.37, 0.41, 0.57, 0.61, 0.51, 0.62, 0.38, 0.72, 0.57, 0.52, 0.49, 0.62, 0.53, 0.43, 0.72, 0.53, 0.82, 0.45, 0.46, 0.59, 0.71, 0.70, 0.58, 0.57, 0.40	0.68, 0.54, 0.49, 0.40, 0.58, 0.71, 0.50, 0.60, 0.58, 0.44, 0.62, 0.33, 0.33, 0.60, 0.41
80–89	0.70, 0.47, 0.57, 0.76, 0.47, 0.51, 0.38, 0.45, 0.70, 0.67	0.63, 0.46, 0.36, 0.72, 0.60, 0.66, 0.59, 0.63

* It is apparent that with the differences in the age distribution of the two groups that an age-sex matched comparison is needed (see Table III).

The segment of the vessel to be measured is pushed gently upward away from the surrounding fat or myocardium and with a minimum of blunt dissection a sufficient length for measurement is exposed. The cone is inserted in the lumen until it completely fills it but does not distend the wall. The post is now adjusted vertically until the proximal cut surface of the artery is at the level of the caliper jaws. The jaws are then moved separately until their tips just touch the external surface of the vessel wall.

While the post is still in the lumen, the external diameter is read by noting on each side the distance traversed by the jaws from mark 0. The sum of these two readings each of which measures the distance from one adventitial surface to the center of the post, is the external diameter of the vessel.

To measure the internal diameter, the calipers are removed from the artery, taking care not to disturb the position of the post and jaws. The jaws are then moved until their tips touch the side of the post and the sum of the distances of the jaws from their respective 0 marks is the internal diameter. The wall thickness for any given segment of coronary artery can be obtained by subtracting the value of the internal from that of the external diameter and dividing by two. The mean wall thickness of the coronary arterial tree can then be obtained by taking the average of the wall thicknesses of all segments measured.

We have found that the wall thickness has seemed to be the most accurate index of the degree of coronary atherosclerosis. Other indices, such as wall volume, wall to lumen ratio and wall area added no further useful information and, indeed, were found to vary considerably with the weight and size of the heart, independent of the amount of coronary arteriosclerosis.

Results

Coronary Wall Thickness: Table II shows the average wall thickness of the coronary arteries of all autopsied East Africans and Americans in the study. It is apparent that, although there are more Africans in the younger age groups, we have a substantial number in the older age groups and that these in general had less arteriosclerosis than the New Yorkers. This observation can be made more easily in the age-sex matched group.

Table III and Figure 2 show the age and coronary wall thickness of forty-three Africans (thirty-four men and nine women) and forty-three Americans forty years of age and over, matched for age and sex.

The average coronary artery wall thickness of the forty-three matched East Africans versus forty-three Americans is 0.31 mm. and 0.50 mm., respectively (difference significant, using Student t test, $p < 0.001$); the average coronary artery wall thickness of East African men versus American men is 0.31 mm. versus 0.52 mm.

TABLE III
Coronary Wall Thickness of Forty-three American and Forty-three African Autopsied Subjects Over Forty Years of Age Matched for Age and Sex

Matched Pair and Sex	Age (yr.)	African Wall Thickness (mm.)	Age (yr.)	New York Wall Thickness (mm.)
1 M	50	0.26	50	0.30
2 M	50	0.25	50	0.41
3 M	45	0.24	46	0.46
4 M	45	0.27	46	0.51*
5 M	70	0.25	70	0.57*
6 M	65	0.27	66	0.56*
7 M	55	0.43	55	0.82
8 M	50	0.27	51	0.45
9 M	40	0.27	40	0.47
10 M	60	0.33	60	0.57*
11 M	70	0.28	70	0.61*
12 M	45	0.24	46	0.28
13 M	50	0.21	53	0.54
14 M	45	0.38	44	0.46
15 M	47	0.23	47	0.73*
16 M	50	0.27	53	0.70*
17 M	60	0.24	60	0.62*
18 M	48	0.30	48	0.57
19 M	45	0.32	43	0.49*
20 M	47	0.37	49	0.30
21 M	60	0.27	60	0.51*
22 M	87	0.49	88	0.76*
23 M	40	0.21	42	0.50
24 M	70	0.57	70	0.51
25 M	67	0.31	67	0.40
26 M	60	0.43	60	0.54
27 M	70	0.52	70	0.38*
28 M	50	0.28	53	0.57
29 M	60	0.43	60	0.58*
30 M	55	0.32	56	0.70
31 M	55	0.30	58	0.38*
32 M	60	0.27	60	0.33
33 M	75	0.31	76	0.59
34 M	60	0.23	60	0.39*
35 F	80	0.28	80	0.46
36 F	68	0.43	68	0.54*
37 F	50	0.23	50	0.33
38 F	62	0.43	62	0.34
39 F	70	0.34	70	0.50
40 F	42	0.27	44	0.30
41 F	65	0.32	65	0.37*
42 F	70	0.32	70	0.60
43 F	60	0.24	61	0.56
Mean of men	56	0.31	56	0.52
Mean of women	63	0.32	63	0.44
Mean of men and women	58	0.31	58	0.50

* Indicates myocardial infarct.

TABLE IV
General Autopsy Data on Subjects over Forty Years Matched for Age and Sex, Mulago Hospital and Albany Medical Center Hospital

Data	Mulago		Albany	
	Men	Women	Men	Women
Body height (inches)	(31) 67	(8) 62	(34) 66.3	(9) 64.4
Body weight (lb.)	(33) 95	(9) 90.2	(34) 155.6	(9) 145.2
Heart weight (gm.)	(34) 230.4	(9) 222.3	(34) 462.5	(9) 385.5
Lung weight (gm.)	(31) 1053.2	(8) 756.2	(34) 1293.8	(9) 915.5
Liver weight (gm.)	(33) 1409.5	(9) 1308.8	(34) 2040.2	(9) 1542.7
Spleen weight (gm.)	(33) 390.0	(9) 216.6	(34) 292.0	(9) 182.7
Brain weight (gm.)	(27) 1230.1	(5) 1186.1	(26) 1370.9	(7) 1244.2

Note. The figures in parentheses indicate the number of cases in which weights were available.

(difference significant, $p < 0.001$); for East African and American women, the average wall thicknesses are 0.32 mm. versus 0.44 mm., respectively (difference significant, $p < 0.025$).

Myocardial Infarcts: In the 137 American hearts there were forty-six infarcts, twenty-nine in men and seventeen in women. Of these, nine hearts (four men and five women) showed recent infarcts only, twenty-nine (twenty-one men and eight women) had old infarcts only, and eight hearts (four men and four women) had both old and recent infarcts. The heart from a thirty-five year old African woman showed a myocardial scar measuring 1.4 by 1 cm. located in the papillary muscle and adjacent myocardium and with diffuse scarring elsewhere. Grossly and histologically this scarring appeared more consistent with healed myocarditis (which is common in the African hearts) than with an infarct. Coronary disease in this subject was negligible.

Coronary Occlusions and Thrombi: In the African coronary arteries, no occlusions, recent or old, were found. In the American series, sixteen hearts showed fresh thrombi (nine in men and seven in women) in coronary arteries. In addition, complete or virtually complete coronary artery occlusion due to an old thrombus or arteriosclerosis was present in sixty-six hearts. In the African hearts, no coronary arterial calcification was seen; 109 American hearts showed one or more foci of calcification. One other observation that was difficult to measure was that such plaques as existed in the African arteries appeared to contain less fat than those plaques in the American arteries. In future studies we will examine these plaques histologically, and particular attention will be paid to their lipid content and possible relationship to syphilis.

Body Height and Weight: A comparison of body heights and weights and of certain organs between the two age and sex-matched groups, African and American, is shown in Table IV. It is obvious that in all weights taken, the American figures are higher. A list showing the major disease as selected by the pathologist in the African autopsy series is shown in Table V. It is apparent that most of the diseases listed are also seen in the United States.

COMMENT

This study confirms by means of direct comparison of tissue and using an objective method of assessing coronary artery wall thickness that coronary arteriosclerosis is of much less severity in autopsied East Africans than in autopsied white subjects in Albany, New York. Differences in age and sex composition of the autopsy populations account only in part for the difference, because in a total of forty-three cases from each autopsy series matched for age and sex, the severity of coronary arteriosclerosis was still significantly greater among white Americans.

Among the 137 New Yorkers, forty-six myocardial infarcts were found; among the forty-three of the matched group seventeen infarcts were found. This is in striking contrast to the complete absence of myocardial infarcts among the African autopsy series.

As can be seen from the scattergrams of American and African coronary arterial wall thickness (Fig. 2), some overlapping of the degree of arteriosclerosis occurs in the two

TABLE V

List of Major Diseases and Their Frequency from 117 East African Autopsied Subjects Aged Sixteen to Ninety-five Years*

Disease	Frequency
Cancer	23
Pneumonia	13
Pulmonary tuberculosis	12
Malnutrition	9
Syphilitic aortitis	9
Anemia of various types	7
Cirrhosis of liver	6
Dysentery	6
Obstetrical complications	4
Pyelonephritis	4
General paralysis of the insane	4
Meningitis	3
Trauma	3
Malaria	2
Typhoid	2
Maladsorption syndrome	2
Poliomyelitis	2
Urethral stricture	2
Diabetes	2
Salpingo-oophoritis	2
Bronchiectasis	2
Intussusception	2
Chronic cholecystitis	2
Tuberculous peritonitis	1
Snake bite	1
Tetanus	1
Cerebral vascular accident	1
Volvulus	1
Encephalitis	1
Secondary amyloidosis	1
Hepatitis	1
Pulmonary aspergillosis	1
Ileal stricture	1
Orbital cellulitis	1
Balantidium coli colitis	1
Nodular hyperplasia of prostate	1
Spinal tuberculosis	1
Peritonitis	1
Alcoholic coma	1
Schizophrenia	1
Senile dementia	1
Essential hypertension	1
Strangulated hernia	1

* In some autopsies it was difficult to decide which was the major diagnosis and in such cases all were included in this list. Hence, the number of diagnoses exceeds the number of cases.

groups. At least some Africans have the same or greater degree of arteriosclerosis as was shown by some Americans who had myocardial infarcts. However, no Africans displayed myocardial infarcts. One explanation for this may be that while a few Africans may have coronary artery arteriosclerosis comparable to that seen in Americans, none have coronary artery thrombosis, which in our experience is the immediate cause of most myocardial infarcts. In a previous study,[4] we have shown that even the incidence of thromboembolic phenomena in the pulmonary circulation was low in East Africans compared with Americans. It is possible that some difference in clotting (or clot lysis) mechanisms is present in the two groups, as has been suggested for South African Bantus and Europeans.[12]

Another possible explanation for the absence of myocardial infarcts in the East African autopsy series, despite the presence of coronary wall thickness comparable to some Americans, is that the arteriosclerosis is of a different type. On gross examination, while difficult to judge objectively, such plaques as existed in the African arteries appeared less yellow and therefore were considered to contain less fat than did the plaques from American arteries. It is possible that the virtual absence of fat in the East African coronary arteries accounted for the absence of occlusive coronary artery disease. The histologic nature of the type of arteriosclerosis in the African autopsy series will be reported in a subsequent paper.

The differences in body height and weight and various organ weights in the two matched groups is possibly a reflection of the different dietary intake of the American group although this statement must be made with reservation since it is difficult to establish the exact dietary intake of either the adult American or East African. It is quite possible that the difference in intake of specific dietary substances, such as fats, may account at least in part, for the different degree of coronary arteriosclerosis in the two groups. It is apparent in Table v that most of the diseases listed are also seen in the United States although the incidences may be different. In a study now in progress, a comparison of diagnoses made at autopsy in 1000 East Africans and 1000 Americans is being carried out.

It is not known how closely the autopsy populations reflect the incidence of diseases in the general population in East Africa and New York State. Factors of selection obviously exist in any autopsy series. However, evidence from all sources (clinical observation, vital statistics and autopsies)[4] indicates a low incidence of myocardial infarcts in East Africa and a high incidence in New York State. In any case, we have available for study two autopsy groups with extreme differences in the occur-

rence of myocardial infarcts. The causes of this difference in incidence are not clear, because of a number of differing circumstances in the two groups. Such things as climate, race, concomitant disease and dietary intake must be considered and much more information must be obtained regarding both the East African and American groups.

As a beginning in obtaining information from these two extreme populations, we are carrying out comparisons of various blood and tissue lipid components. There is no certainty that the answer to the differing severity of coronary arteriosclerosis and incidence of myocardial infarcts lies in possible differences in lipid patterns. However, such information should add to our basic store of knowledge regarding relationships of lipid patterns and arteriosclerosis.

Summary

A comparison of the degree of coronary arteriosclerosis and number of myocardial infarcts in 117 autopsied East Africans and 137 New Yorkers was made. In forty-three subjects from each series (thirty-four men and nine women) matched for age and sex, the amount of coronary arteriosclerosis was generally much higher in the New York autopsy series, although the East Africans were not free from arteriosclerosis, and some overlapping occurred between the two groups. In this same matched group there were seventeen myocardial infarcts among the Americans, while none were found in the East African autopsy series.

Comparative studies of blood and tissue lipid patterns, as well as clot lysis in the two groups, are now being carried out in an attempt to obtain other information pertaining to these findings.

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The Comparative Racial Prevalence of Ischemic Heart Disease in Cape Town*

VELVA SCHRIRE, M.B., CH.B. (Cape Town), M.R.C.P., F.R.C.P.E.

Cape Town, South Africa

IN PREVIOUS publications from this laboratory[1–4] the rarity of ischemic heart disease in the Bantu of Cape Town was described. The information was obtained from both clinical and necropsy evidence. Thus, by 1957 only three cases of cardiac infarction in the Bantu had been recognized electrocardiographically over a six year period. Necropsy evidence of cardiac infarction on the basis of coronary atheroma was found in only one case. On the other hand, ischemic heart disease was encountered extremely commonly in the whites, whereas the incidence in the Cape colored fell between that of the white and the Bantu.

Working with the same population group in Cape Town and drawing his material from the same source, Sacks[5] has confirmed these findings at necropsy. Careful postmortem examination and grading of the degree of atheroma showed that although on occasion severe aortic and coronary atherosclerosis did occur in the Bantu, it was much less common than in the whites. Severe luminal narrowing of the coronary arteries was particularly rare in the Bantu, in keeping with the rarity of myocardial infarction. Sacks was particularly impressed to find complete freedom from atherosclerosis in the aorta and coronary arteries of the Bantu at ages in which it was rare to find such freedom in whites. The difference between the whites and Negroes was far less striking than between the whites and Bantu. The rarity of cardiac infarction in the Bantu has been well established elsewhere in South Africa,[6–9] Southern Rhodesia,[10] Uganda[11] and West Africa.[12]

The only exceptions to this general experience have been the reports from Laurie et al.[13,14] from Pietermaritzburg, Natal. These investigators report the frequent finding of ischemic heart disease clinically.[13] At necropsy atherosclerosis of the aorta, cerebral hemorrhage and thrombosis were common,[14] coronary atherosclerosis was a frequent finding, sometimes of a severe degree, and five cases of "frank infarction" were encountered.[13] Their observations suffer from the fact that they were working with Bantu patients only and were unable to compare their findings in the Bantu with those of other races. Pepler and Meyer[15] in a well designed and controlled necropsy study of the heart in whites and Bantu, have demonstrated a significantly better coronary anastomotic blood supply in the hearts of the Bantu from a very early age, confirming Laurie and Woods' findings in normal Bantu.[16] However, they reaffirm the low incidence of severity of coronary atherosclerosis and its complications in the Bantu.

It is the purpose of this paper to present further supportive electrocardiographic evidence of the low incidence of ischemic heart disease in the Bantu compared with the colored and white races.

MATERIAL AND METHODS

As in previous reports[1,2] the material was drawn from Groote Schuur Hospital and the New Somerset Hospital which have an approximately equal number of whites and nonwhites. Figures compiled from the Bureau of Census and Statistics for 1957 reveal that the population of Metropolitan Cape Town consisted of 280,800 Europeans, 351,100 Cape colored and 67,800 Bantu, giving a proportion of 4 : 5 : 1, respectively. Thus, even taking the question of age into consideration, there are more nonwhites at risk than whites. The population of the hospital, however, is selected, because a means test prevents the attendance of all but the poorest section of the community. Almost all the nonwhites are eligible and this certainly applies to the Bantu; however only the less economically privileged whites are eligible. It is generally accepted that ischemic

* From the Cardiac Clinic, Groote Schuur Hospital and C.S.I.R. Cardio-Pulmonary Research Group, Department of Medicine, University of Cape Town, Cape Town, South Africa.

TABLE I

Racial Incidence of Myocardial Infarction Determined Electrocardiographically in 1958 (A) and 1959 (B) (Rigid Criteria)

	Race	Racial Distribution of Electrocardiograms		Racial Distribution of Infarct Patterns		Percentage of Racial Distribution of A:308 Infarcts; B:412 Infarcts	Percentage of Electrocardiograms Showing Infarcts
		Number	Ratio	Number	Ratio		
A	White.....	2,256	7.3	235 (152)	117	76.3	10
	Colored.....	1,705	5.6	71 (46)	35	23	4.2
	Bantu.....	307	1	2 (2)	1	0.6	0.6
	Total.....	4,268		308			
B	White.....	2,694 (2,037)	7	315 (209)	315	76.5	12
	Colored.....	2,160 (1,870)	5.6	96 (78)	96	23.25	4.4
	Bantu.....	385 (353)	1	1 (1)	1	0.25	0.3
	Total.....	5,239		412			

NOTE: The figures in parentheses refer to new patients seen for the first time.

heart disease is commoner in the economically privileged so that, if anything, the prevalence of ischemic heart disease in the white at large is underestimated by the figures obtained in our hospitals.[18]

During 1958 and 1959 attendances of patients of all ages at the General Outpatients' section totaled 684,553, of which 391,747 were colored and Bantu, the remaining 292,806 being white; 37 per cent attended for the first time. Of the adults admitted to the Wards of Groote Schuur Hospital, 19,588 were Colored, 4,311 Bantu and the remaining 21,411 white.

It is fair to conclude that the number of nonwhites with ischemic heart disease should at any rate equal that of the whites if ischemic heart disease were equally prevalent in all races. Although the Bantu population in this group is only a quarter of the white, a significant number of Bantu patients with ischemic heart disease should appear. This is valid even though the Bantu population is a highly selected one (Tables I and IV).[1,2]

As in previous years[1,2] the electrocardiographic service of the Cardiac Clinic was available to all in- and outpatients attending Groote Schuur Hospital and the forty-four inpatient teaching beds of the New Somerset Hospital. Electrocardiograms in all cases included the six limb leads and precordial leads V_1 to V_7. Since all records were interpreted by two physicians (at least 80 per cent by the author) any errors in electrocardiographic interpretations were constant for all races and the facilities for obtaining electrocardiographic investigations were equal. The data should therefore reflect the relative prevalence of the disease as it occurs in these hospitals.

Diagnostic Criteria: Rigid criteria were used for the diagnosis of myocardial infarction.[1] Abnormal T wave and S-T segment changes alone were not accepted. Thus, the presence of wide or deep Q waves in the precordial leads or diminution of R waves across the precordium with T wave inversion or S-T segment changes was required. In inferior infarction a Q wave of at least 0.04 second in width or deeper than 30 per cent of the R wave in aVF was accepted. In the presence of right bundle branch block a Q wave of 0.04 second in aVF or abnormally wide Q waves in the precordial leads indicated infarction. Infarction was very seldom diagnosed in the presence of left bundle branch block, unless Q waves or definite S-T segment depression over the left ventricle were present. These criteria have been found to give a 96 per cent accuracy.[1]

Less rigid criteria[18] were the presence of T wave inversion without Q waves over the anterolateral or posterior aspects of the left ventricle, or bundle branch block without significant Q waves or S-T segment shift. As these criteria alone gave only a 75 per cent accuracy[1] a history of angina pectoris or cardiac infarction was demanded in addition. Patients with normal tracings were not considered in this analysis.

RESULTS

During 1958 there were 4,268 patients, the ratio of white to colored to Bantu being 7.3 : 5.6 : 1. During 1959 there were 5,239 patients, the ratio being 7 : 5.6 : 1. If only patients over the age of thirty years were considered the racial distribution of electrocardiograms in the whites, colored and Bantu was approximately the same, 7.9 : 5.3 : 1 (3,353 patients) and 7.8 : 5.2 : 1 (4,224 patients), respectively (Table II).

Of the 9,507 patients, 720 showed the classic pattern of myocardial infarction, 308 in 1958 and 412 in 1959. Of these, 550 (76 per cent) were in whites and 167 (23 per cent) in colored

TABLE II

Racial Incidence of Ischemic Heart Disease Determined Electrocardiographically in 1958 (A) and 1959 (B)

	Race	Racial Distribution of Electrocardiograms		Racial Distribution of Abnormal Patterns		Percentage of Racial Distribution of A:712 Cases; B:867 Cases	Percentage of Abnormal Electrocardiograms
		Number	Ratio	Number	Ratio		
A	White.....	2,256	7.3	522 (328)	104	73	23
	Colored.....	1,705	5.6	185 (128)	37	26	11
	Bantu.....	307	1	5 (5)	1	1	1.6
	Total.....	4,268		712			
B	White.....	2,694 (2,037)	7.0	624 (406)	78	72	23
	Colored.....	2,160 (1,870)	5.6	235 (179)	40	27	11
	Bantu.....	385 (353)	1	8 (6)	1	1	2
	Total.....	5,239		867			

NOTE: The figures in parentheses refer to new patients seen for the first time.

(Table I). There were three cases in the Bantu (0.4 per cent).

There were an additional 859 cases in which a history of angina pectoris or cardiac infarction was present with an abnormal electrocardiogram, 404 in 1958 and 455 in 1959. Of these, 596 were in whites, 253 in colored and ten in Bantu. The total number of electrocardiograms showing evidence of "ischemic heart disease" therefore was 1,579, of which 1,146 were in whites, 420 in colored and thirteen in Bantu (Table II).

Effect of Age and Sex: The distribution of cardiac infarction by decade from thirty years and over among the three racial groups is shown in Table III and of ischemic heart disease, in Table IV. The sex distribution is shown in the same tables.

COMMENTS

The difference in the prevalence of ischemic heart disease among the three racial groups has again been confirmed. If the data obtained by using strict electrocardiographic criteria are analyzed (Table I), three times as many cases occur in the whites as in the colored (550 : 167) and this applies to new as well as old patients. Almost the same incidence is obtained if the electrocardiographic criteria for the diagnosis of ischemic heart disease are less rigid (1,146 : 420). These findings are almost identical to those found from 1952 to 1957.[1,2] The figures are even more striking in the case of the Bantu, only three of 692 patients showing the pattern of cardiac infarction and thirteen that of ischemic heart disease.

The difference in incidence cannot be ascribed to the fact that more electrocardiograms were taken in whites than in nonwhites (4,950 : 4,557). By expressing the number of infarctions as a percentage of the total number of electrocardiograms taken in each racial group, the actual difference is well shown (Tables I and II). Thus, 100 electrocardiograms in whites include eleven (rigid criteria) or twenty-three infarctions (less rigid criteria); 100 electrocardiograms in colored show four and eleven, respectively; whereas 100 electrocardiograms in Bantu include only 0.4 and two, respectively. Neither can the difference in incidence be attributed entirely to an age factor[1] (Tables III and IV). Both in the whites and Cape colored over 85 per cent of cases occurred in persons forty years of age and over. The peak incidence in whites occurred between the ages of fifty and sixty-nine years, the maximum number of cases occurring in the decade sixty and sixty-nine. In colored the peak incidence was likewise between fifty and sixty-nine years but the peak decade was fifty to fifty-nine years. With regard to the effect of sex on the incidence of cardiac infarction (Tables III and IV), it is evident that during the reproductive cycle (twenty to forty-nine years) the incidence in men far outnumbers that in women in all races. With advancing age the women begin to catch up with the men and after seventy may even exceed them. Ischemic heart disease has at last been encountered in the Bantu woman in Groote Schuur Hospital as was only to be expected with increasing data. Until 1958 no case had yet been recorded in the Bantu woman al-

TABLE III

Age and Sex Distribution of Cardiac Infarction Patterns in 488 Cases in White, Colored and Bantu during 1958 and 1959 (New Patients Only)

Age (yr.)	White				Colored				Bantu			
	Male	Female	M/F Ratio	Total	Male	Female	M/F Ratio	Total	Male	Female	M/F Ratio	Total
Under 30	1	...	...	1	2	...	...	2	...	...	...	3
30–39	16	4	4:1	20	12	...	...	12	...	...	...	32
40–49	44	6	7:1	50	20	4	5:1	24	...	...	...	74
50–59	74	21	3.5:1	95	33	10	3:1	43	2	1	2:1	141
60–69	74	35	2:1	109	22	9	2:1	31	...	...	...	140
70+	46	40	1:1	86	5	7	1:1	12	...	...	...	98
Total	255	106	2.5:1	361	94	30	3:1	124	...	...	...	488

TABLE IV

Age and Sex Distribution of Ischemic Heart Disease in 1,054 Cases in White, Colored and Bantu during 1958 and 1959

Age (yr.)	White				Colored				Bantu			
	Male	Female	M/F Ratio	Total	Male	Female	M/F Ratio	Total	Male	Female	M/F Ratio	Total
Under 30	1	...	...	1	2	...	...	2	...	...	...	3
30–39	28	8	3.5:1	36	16	4	4:1	20	1	...	...	57
40–49	65	33	2:1	98	42	28	1.5:1	70	1	1	1:1	170
50–59	112	73	1.5:1	185	63	47	1.3:1	110	3	3	1:1	301
60–69	131	101	1.3:1	232	44	31	1.3:1	75	1	...	...	308
70+	92	92	1:1	184	13	17	1:1.3	30	1	...	...	215
Total	429	307	...	736	180	127	...	307	7	4	...	1,054

TABLE V

Comparative Racial Prevalence of Myocardial Infarction Determined Electrocardiographically (Rigid Criteria) during the Years 1952 to 1959 (New Cases)

Race	1952 to 1956			1957			1958 to 1959		
	No. of ECG's	No. of Infarct Patterns	Percentage of Racial Distribution of 991 Infarcts	No. of ECG's	No. of Infarct Patterns	Percentage of Racial Distribution of 214 Infarcts	No. of ECG's	No. of Infarct Patterns	Percentage of Racial Distribution of 488 Infarcts
White	7,232	760	76.6	1,966	161	75	4,950	361	74
Colored	4,397	228	23.1	1,338	53	25	3,865	124	25.4
Bantu	783	3	0.3	221	0		692	3	0.6

though well documented elsewhere in South Africa.

The results obtained in this study confirm the presence of a considerable difference in the incidence of ischemic heart disease among the three racial groups. The whites far outnumber the Bantu, and Cape colored fall between the two groups. A comparison with the findings of previous years (Table v) shows that there has been virtually no change in the prevalence of the disease measured electrocardiographically in the three racial groups during the years 1952 to 1959.

All workers in this field[1,5,6–9,15] accept the

fact that cardiac infarction does occur in the Bantu but only rarely. Even Laurie et al.[13] concede that it occurs less commonly than in the whites. Similarly, it is accepted that coronary atheroma occurs in the Bantu,[2,5,8,15] but this is less extensive and severe than in the white. It is another thing, however, to attribute cardiac failure to coronary atheroma on the basis of nonspecific electrocardiographic abnormalities and patchy fibrosis of the myocardium and coronary atherosclerosis.[13] Cardiac failure of obscure origin is common in the Bantu,[9,19,22] and until our knowledge and understanding about these conditions improve, it would be better to regard them as cryptogenic or unknown than to ascribe them to coronary atherosclerosis.

Summary

1. Electrocardiograms of 9,507 patients attending the Groote Schuur Hospital in Cape Town during the years 1958 and 1959 were analyzed to determine the racial incidence of myocardial infarction.

2. Electrocardiographic evidence of coronary disease was very uncommon in the Bantu, occurring in only three patients; in an additional ten cases there was a history of coronary disease associated with an abnormal tracing.

3. Electrocardiographic evidence of myocardial infarction and ischemic heart disease was found far more commonly in whites than in Cape colored, in both of whom the disease was common.

4. The results confirm previously reported studies from Cape Town and elsewhere in the Union of South Africa.

Acknowledgment

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Acute Myocardial Infarction in Ninety Negro Patients: Clinical Manifestations and Immediate Mortality

Comparison with 229 Similarly Studied White Patients*

JOHN THOMAS, M.D., CALVIN CALHOUN, M.D., CON O. T. BALL, R. S. ANDERSON, M.D. *and* GEORGE R. MENEELY, M.D., F.A.C.C.

Nashville, Tennessee

THERE have been many varied and conflicting reports in the literature concerning the clinical manifestations and incidence of acute myocardial infarction in the Negro.

The impression that the characteristic symptom of pain is less frequent is still widespread although this has not been substantiated by clinical studies. Dyspnea has been described as the most frequent presenting symptom. Results of studies on the incidence of acute myocardial infarction in the Negro due to atherosclerosis have varied from ratios of 4 : 1 to 4 : 3 more common in whites.[1,2] Still others have reported no difference in the incidence in Negroes and whites.[3] As late as 1946 Hunter[4] called attention to the fact that he was unable to find in the literature an adequate description of the clinical picture of myocardial infarction in the Negro. He further stated that the diagnosis was rarely made clinically in this group because the clinical picture was different. His opinion was that this disease was as common in the Negro as in white persons of comparable age groups but that the diagnosis was obscured in the Negro because dyspnea is the chief complaint and pain is absent. This conclusion regarding the clinical picture was reached after reviewing 1,000 consecutive autopsies on Negroes and 1,000 consecutive autopsies on white patients of the Louisville General Hospital over a ten year period. Even at George W. Hubbard Hospital of Meharry Medical College which cares only for Negro patients, acute myocardial infarction was, at one time, considered a rarity. Writings and teachings of previous years to the effect that myocardial infarction is rare in Negroes have made physicians less alert to the possibility in this group and have thereby tended to perpetuate as fact an assumption that may be entirely incorrect. It is believed that a report on the clinical observations of acute myocardial infarction from a hospital which cares only for Negro patients, would, at this time, be of value in further delineation of the incidence and clinical manifestations of this important disease. Comparisons have been made with the findings in 229 similarly studied white patients.[5]

MATERIAL AND PROCEDURE

The records of all patients at George W. Hubbard Hospital, Meharry Medical College, with a diagnosis of acute myocardial infarction during the last twenty-five years were reviewed. The data were coded and transferred to International Business Machine punch cards, making available for each patient over 500 particulars concerning the clinical manifestations, physical findings, laboratory analysis, past history, family history and socioeconomic status.

One or more of the following criteria were required for inclusion in the study: (1) Typical clinical manifestations, usually consisting of prolonged precordial, epigastric or substernal pain, frequently accompanied by signs of shock, elevation of temperature, leukocytosis, fever and acceleration of the

* From the Department of Medicine, Meharry Medical College, and the Departments of Medicine and Preventive Medicine and Public Health, Vanderbilt University School of Medicine, Nashville, Tennessee. This work was supported in part by a training grant, HT-502, National Heart Institute, National Institutes of Health, Public Health Service; the United Givers Fund of Greater Chattanooga; the Federal Aviation Agency (FA-1766); and the Army Medical Research and Development Command (DA-49-193-MD-2067).

erythrocyte sedimentation rate; (2) electrocardiographic changes clearly indicative of acute local myocardial infarction with or without typical clinical manifestations; (3) the demonstration at autopsy of a recent myocardial infarction with or without a completely occluded coronary artery.

Ninety patients, fifty men and forty women, met one or more of the above criteria. One patient, a thirty-six year old female, had the onset of myocardial infarction during an episode of acute rheumatic fever. All of the other cases are presumed to be due to atherosclerosis. Data from only one attack were compiled in each case. The attack described was the first attack in eighty individuals, second attack in three and unknown in seven. The number of the subject attack was said to be unknown when areas of old and recent myocardial infarction were found at autopsy.

The incidence, clinical manifestations and immediate mortality (death within thirty days) were compared with a twenty-five year similar study of 229 white patients at Vanderbilt University Hospital in the same geographic area.[5] Both studies were conducted by some of the same investigators, who observed the clinical course in most of the cases presented.

Significance was determined by chi square, the measure of the difference between samples and was designated for a probability of less than 0.05. If chi square probability approached the 0.05 level, the difference between the samples was termed suggestive.[6]

Findings

INCIDENCE

Seventy-seven of the ninety cases were diagnosed during the last ten years of the study. It is believed that the increase in incidence during the last ten years is due to a larger number of patients admitted (during this period the hospital was converted from a predominantly private hospital to a predominantly city hospital), more awareness of the disease and alertness on the part of the physicians at the hospital, better diagnostic tools (including more frequent use of electrocardiography and the introduction by LaDue et al.[7] of the serum transaminase determination) and an increased tendency for hospitalization on the part of both physicians and patients. That these factors are very important is evident in the observation that over the last five years there were forty-nine patients found to have acute myocardial infarction. During the first fifteen years only thirteen cases were found. It is unreasonable to assume that this represents an actual increase in the incidence of the disease. For the last five years the medical service at this hospital has had approximately sixty beds. The number of individual admissions over this period of time is not available, so that the exact incidence of this entity cannot be determined. However, forty-nine patients with acute myocardial infarction over a period of five years on a sixty bed general medical service leaves no doubt of the occurrence of this disease in the Negro.

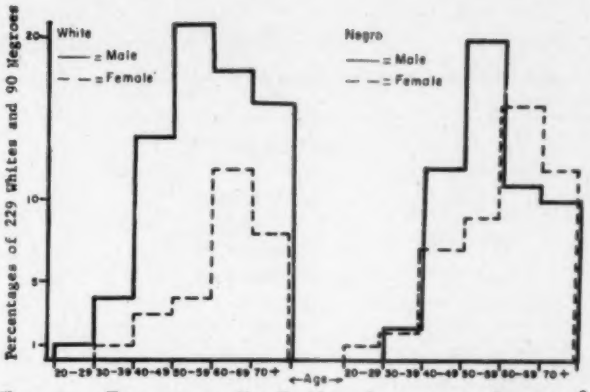

FIG. 1. Frequency distribution by age and sex of ninety Negro and 229 white patients with myocardial infarction.

SEX AND AGE INCIDENCE

Fifty patients were males and forty were females. In the white series of 229 patients, 168 were males and sixty-one were females (Fig. 1). The mean age at the time of the attack for Negro males was fifty-seven and for white males was fifty-eight; for the Negro females it was sixty-one and for the white females, sixty-four years. This differs from the generally held view that the age of onset is earlier in the Negro than in the white. It would seem also clinically not to support the observation of the autopsy studies of Blache and Handler[8] whose comparison of the arteries of corresponding age groups of whites and Negroes led to the conclusion that the rate of development of coronary arteriosclerosis in the Negro was slower than in the white by approximately ten years.

IMMEDIATE MORTALITY

Among the Negro patients the immediate mortality, 26 per cent, was significantly lower than in the white, 41 per cent. Mortality in the Negro was not sex specific (males 26 per cent, females 25 per cent). Mortality among white females, 48 per cent, was higher than among males, 39 per cent.

SEASONAL INCIDENCE

There was no significant difference in the seasonal incidence. In the Negro the incidence

TABLE I
Past History Relative to Cardiovascular System and Diabetes Mellitus

History	Total					Male		Female	
	Presence or Absence Known	No.	Per Cent	Immediate Mortality		No.	Per Cent	No.	Per Cent
				No.	Per Cent				
Hypertension	55	43	78	8	19	23	53	20	47
Angina pectoris	80	63	79	14	22	34	54	29	46
Congestive failure	88	30	34	10	33	17	57	13	43
Diabetes	90	13	14	4	31	2	15	11	85

was lowest in the fall. In the white group the lowest incidence was in the spring.

ACTIVITY AT TIME OF ATTACK

The type of activity at the time of attack was known in fifty-three of the subjects. As in the white study most of the attacks (twenty-seven) occurred during complete rest or inactivity. Twelve occurred during slight activity and fourteen occurred during moderate activity. Nine had attacks less than two hours after eating.

HISTORY OF CARDIOVASCULAR DISEASE

Angina Pectoris: Sixty-three of the eighty subjects or 79 per cent in whom the past history was known described angina pectoris prior to the current attack (Table I). The incidence was practically the same in both sexes. The incidence of angina prior to the attack was significantly higher than the 54 per cent found in the white group.

Hypertension: A history of hypertension (persistent elevation of blood pressure above 150 mm. Hg systolic and 90 mm. Hg diastolic) was found in forty-three of the fifty-five subjects in whom the character of the blood pressure preceding the attack was known. This represents an incidence of 78 per cent. In the white series the blood pressure prior to the attack was known in 215 subjects. One hundred thirteen or 53 per cent were hypertensive. This is significant and confirms the high incidence of hypertension in Negro patients with myocardial infarction as reported by Weiss and Gray.[9]

Congestive Failure: Thirty or 34 per cent of the patients had a history of congestive failure prior to the current attack. The immediate mortality in this group was significantly high. This is similar to the finding in the white group.

SYMPTOMS WITH THE ATTACK

Symptoms with the attack, except angina pectoris, are presented in Table II and compared with the incidence and immediate mortality in the white group. Generally they are similar except for a lower immediate mortality in the Negro group.

Angina Pectoris: Pain during the acute attack of myocardial infarction has been the subject of much discussion. Pain was present in seventy-seven of the ninety patients or 85 per cent as compared with 90 per cent in the white group. Thirteen or 14 per cent of the Negro patients were described as having no pain; however, all of these patients were either unconscious or irrational due to cerebrovascular accident, postoperative shock, diabetic acidosis, hypoglycemia, or were in severe congestive heart failure.

Dyspnea: More than half of the Negroes were found to have dyspnea during the current attack. This symptom was present in 70 per cent of the white group. In some instances the dyspnea was so marked that it was of more concern to the patient than the pain but not to the exclusion of pain. When it occurred to this extent, the patients were invariably in congestive heart failure. Dyspnea with the attack was described in 35 per cent of the Negro soldiers with acute myocardial infarction reported by Yater et al.[3]

PHYSICAL FINDINGS WITH THE ATTACK

Congestive Failure: Forty-three or 47 per cent of the patients had or developed congestive

TABLE II
Symptoms with Attack
Incidence and Associated Immediate Mortality in Ninety Negro and 229 White Patients

Symptom	Negro				White			
	Incidence		Immediate Mortality		Incidence		Immediate Mortality	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Dyspnea	49	54	10	20	160	70	77	48
Restlessness	59	65	13	22	90	39	41	46
Weakness	38	42	7	18	86	38	37	43
Nausea	26	29	4	15	82	36	32	39
Vomiting	29	32	5	17	76	33	30	39
Sweating; clammy	39	43	11	28	65	28	45	69
Cough	7	8	2	29	62	27	29	45
Cloudy sensorium	16	18	6	38	62	27	42	68
Vertigo	5	6	1	20	15	7	6	40
Palpitation	5	6	3	60	16	7	5	31
Fatigue	4	4	1	25	17	7	6	35

failure during the acute attack. The immediate mortality in this group was 33 per cent. This is the group in which the presence of pain may be overshadowed by troublesome dyspnea. Other physical findings were not significantly different from those of the white group. The variation of the physical findings may be due to inadequate examination. Of note is the absence of auricular fibrillation in the Negro subject as compared with an incidence of 11 per cent among the white. As in the white group an increase in the immediate mortality was associated with an increase in pulse rate, leukocytosis and temperature elevation.

Behavior of Blood Pressure during Attack: The character of the blood pressure during the first twenty-four hours of the attack was adequately described in fifty-five subjects. The immediate mortality was significantly higher in patients who had a fall in pressure than in those who showed no fall. Nineteen of the patients had a fall of more than 50 mm. Hg. This group was associated with the highest immediate mortality.

Luetic Heart Disease: Three patients had findings compatible with the diagnosis of luetic heart disease. This was assumed to be only a concomitant finding. There was nothing to suggest coronary ostial involvement.

Diabetes Mellitus: Thirteen patients or 14 per cent of the subjects with acute myocardial infarction had diabetes mellitus (Table I). Eleven were females and only two were males. Except for one female all of these patients gave a history of angina pectoris. The blood pressure preceding the attack of myocardial infarction was known in eleven of the subjects. Nine had hypertension. Eight of the twelve diabetic patients in whom the presence or absence of congestive failure was known, had this finding. The incidence of hypertension and congestive heart failure was higher than in the series as a whole. Four of the thirteen patients died within thirty days of the acute attack.

EFFECT OF TIME OF HOSPITALIZATION

The immediate mortality of patients who had the attack while hospitalized was very high. Of eighteen who were already in the hospital nine or 50 per cent died within thirty days. The immediate mortality of patients brought to the hospital within twenty-four hours was 14 per cent or seven of forty-eight patients. It is not surprising that the further insult of myocardial infarction occurring in an individual already ill with another disease was frequently lethal.

COMMENTS

A high index of suspicion is necessary for the diagnosis of myocardial infarction and is in part responsible for the increase noted at this hospital. A patient, understanding historian will frequently uncover the true nature

of vague complaints in a stoic individual. The high incidence of angina pectoris is contrary to most impressions. Its presence and characteristics were similar to those of the white group. These findings agree with Yater et al.[2] who found the presence of pain in 76.2 per cent of sixty-three Negroes with acute myocardial infarction. The intensity of pain was interpreted as severe, moderately severe and mild. As with the white group the immediate mortality increased with the severity of the pain. There was no instance in which a "silent" myocardial infarction could be documented. Pain is a subjective symptom and its description varies with the individual. The character of the pain in most instances as with the white group was described as constricting or crushing. The high incidence of dyspnea and congestive failure in the group might have influenced the description of the pain. With the onset of congestive failure, dyspnea may take precedence over the previous pain if the patient is not questioned carefully. The lack of an adequate vocabulary to express feelings may be another barrier. For instance, some patients denied having pain but admitted to a "hurting" in the chest. The true nature of the symptoms was brought out only after careful questioning and a show of concern on the part of the physician. Also the word "indigestion" was used by some patients to describe the pain. This is common and may often be misleading.

The finding of a nearly equal sex distribution of myocardial infarction in the Negro in this study has been supported by studies of other observers.[10,11] This may be due to the high incidence of hypertension in the Negro female. Also the high incidence of diabetes mellitus in the females as compared with males may be significant in causing an increase of the disease in the former. The immediate mortality was significantly lower in the Negro. The exact reason for this cannot be explained. It is possible as has been suggested by Hunter[4] that hypertension leads to the development of a more adequate collateral coronary circulation and thus spares the myocardium of the Negro. On the other hand hypertension is considered as one of the parameters responsible for an increased incidence of myocardial infarction in the Negro female.

Summary

1. The records of ninety Negro patients with acute myocardial infarction have been reviewed.

2. The findings indicate that a higher index of suspicion would lead to more frequent diagnosis and better treatment of this potentially fatal disease in the Negro.

3. The clinical manifestations, age-sex incidence, laboratory findings and immediate mortality rate (death within thirty days) have been compared with those of a similarly studied group of 229 white patients in the same geographic area.

4. Generally the clinical manifestations were the same in the two groups.

5. The incidence of precordial pain as a presenting symptom was 85 per cent in the Negro group and 90 per cent in the white group.

6. The sex incidence in the Negro series was almost equal whereas in the white series the ratio of males to females was 3:1.

7. A higher incidence of hypertension was found among the Negroes.

8. A higher incidence of diabetes mellitus was found among females, both in the Negro and the white patients.

9. The immediate mortality was lower among the Negro patients, 26 per cent, than among white patients, 41 per cent.

Acknowledgments

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The Normal RS-T Segment Elevation Variant*

RICHARD H. WASSERBURGER, M.D. *and* WILLIAM J. ALT,† M.D. WITH THE TECHNICAL ASSISTANCE OF CAROLINE J. LLOYD

Madison, Wisconsin

THE NORMAL precordial RS-T variant, first described by Myers et al.[1] and later stressed by Goldman,[2] continues to challenge the clinician because of its gross similarity to the injury potential of an acute pericarditis or myocardial episode.

This normal variant consists of the following: (1) an elevated take-off of the S-T segment at the J junction of the QRS complex, varying from 1 to 4 mm. relative to the succeeding T-P interval (isoelectric line); (2) a downward concavity of the S-T segment; and (3) symmetrically limbed T waves which are often of large amplitude. This pattern is usually seen in the mid- and left precordial leads V_3, V_4 and V_5. Goldman[2] stressed that this variant occurred most commonly in the young Negro patient, and he, as well as others, have reported that the S-T elevation returns to the isoelectric line after exercise. Accelerated ventricular repolarization has generally been held as the mechanism of this phenomenon.[1-3]

The purpose of this manuscript is to reemphasize the over-all electrocardiographic pattern of the normal RS-T segment variant, to show the effects of exercise and hyperventilation upon it, and to stress its similarity to the changes of epicardial potential noted in pericardial and myocardial disease.

MATERIALS AND METHODS

Electrocardiograms were available of forty-eight patients with RS-T segment elevation greater than 1 mm. in two or more precordial leads, V_3 through V_6. There was no clinical evidence of heart disease in any of these patients. This represents an incidence of 1 per cent for all hospital admissions over a seven year period at the Veterans Administration Hospital, Madison, Wisconsin. Of these forty-eight patients, thirty-five were Negro and thirteen were Caucasian. The mean ages were thirty-two and forty-three years, respectively, and the over-all range in age was from twenty-two to sixty-nine years.

Twenty-four patients were exercised by running in place to the point of fatigue with subsequent electrocardiographic survey. Twenty-seven patients completed the hyperventilation procedure, which consisted of electrocardiographic monitoring following ten to fifteen seconds of brisk hyperventilation. Serial electrocardiograms of most patients were available during prolonged courses of hospitalization.

In addition, individual patients are presented with clinically evident pericardial and myocardial disease whose electrocardiograms simulated those of the normal RS-T segment variant.

All electrocardiograms were taken in recumbency, utilizing the Sanborn Viso-Cardiette.

RESULTS

The electrocardiographic tracings of the forty-eight patients with "normal RS-T segment variants" could readily be placed into one of two groups—Group 1: thirty-seven patients exhibiting elevated S-T junctions in leads V_3, V_4, V_5 (reflecting anterior wall potentials), associated with counterclockwise rotation of the precordial QRS complexes (Fig. 1); Group 2: eleven patients presenting the S-T segmental shift in leads II, III, aVF, V_5 and V_6 (reflecting posterolateral wall potentials) (Fig. 2). This grouping was independent of electrocardiographic cardiac position. The reproducibility of these two patterns from patient to patient was striking and, in general, the degree of S-T segmental elevation was of greater magnitude in Group 1. Although the elevated S-T junction arose from a distinct notch on the downstroke of the R wave in most instances, occasionally it would be represented only as a

* From the Department of Medicine, Veterans Administration Hospital and the Cardiovascular Laboratory of the Department of Medicine, University of Wisconsin Medical School, Madison, Wisconsin.

† Present address: Muskegan, Michigan.

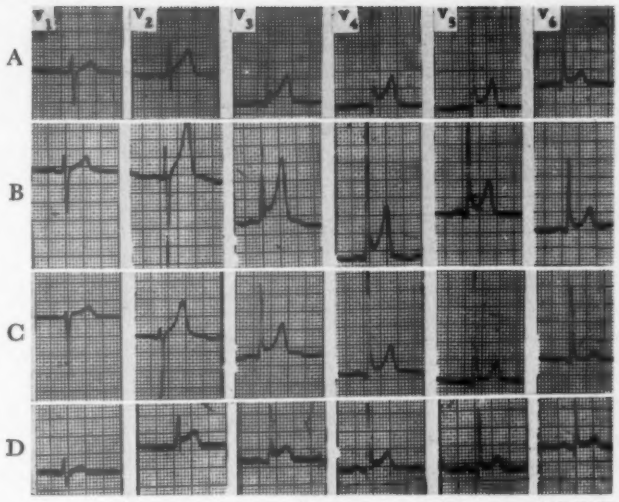

FIG. 1. Four examples of Group 1. The normal RS-T segment variant characteristically seen in precordial leads V_3, V_4, V_5 and V_6, usually maximum in V_3 and V_4. Note the consistent finding of left ventricular potential in V_3 in this group, denoting counterclockwise rotation. A, a thirty-two year old Negro. Stable pattern over a nine month period. B, a twenty-six year old Negro. C, a forty-six year old Caucasian. D, a thirty year old Negro. Stable pattern over a six month period.

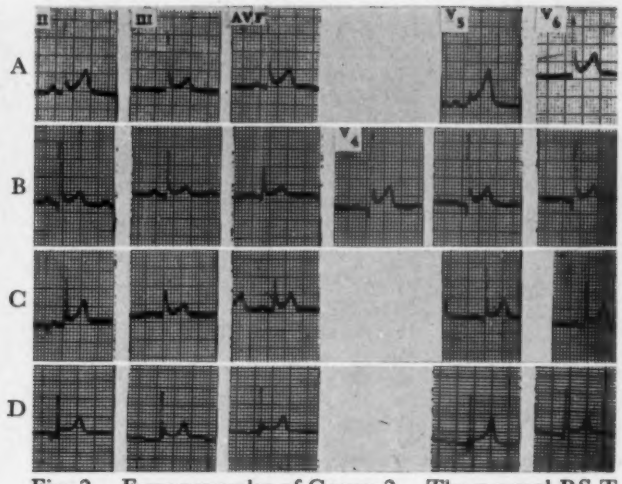

Fig. 2. Four examples of Group 2. The normal RS-T segment variant less frequently presents in leads II, III, aVF, V_5 and V_6, reflecting potential from the posterolateral wall of the left ventricle. The counterclockwise rotation is not seen in this group. A, a twenty-six year old Negro. Stable pattern over a six and a half month period. B, a thirty year old Negro. Stable pattern over a six month period. C, a thirty-two year old Caucasian subject. D, a forty-eight year old Caucasian subject. Stable pattern over a six year period.

well-defined slur. Thus, it superficially resembled a reversed Wolff-Parkinson-White pattern with notching at the distal segment of the QRS complex rather than at its inception, implying accelerated ventricular repolarization.

Exercise: Contrary to the results of Goldman,[2] Chelton and Burchell,[3] Chapman and Overholt,[4] and Diestel et al.,[5] who uniformly noted prompt return of the elevated S-T segment to the isoelectric line following exercise, only fourteen of twenty-four patients so studied showed this change (Fig. 3). The remaining

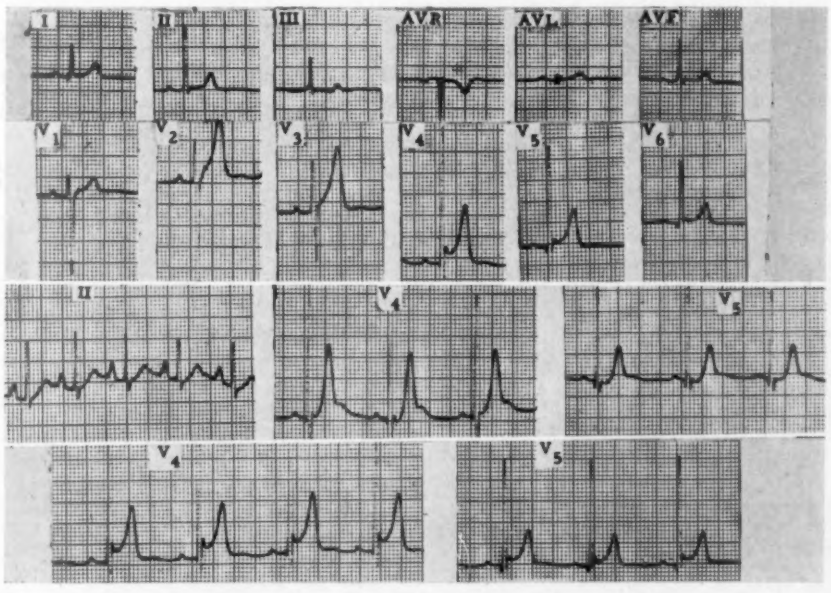

Fig. 3. *Effect of exercise.* The elevated RS-T segment variant seen in V_4 and V_5 appears to have approached the isoelectric line following exercise (middle strip). A rather prominent Ta wave is shown in standard lead II immediately following exercise. The elevated RS-T segment returned to the control level within five minutes following exercise (bottom strip). Electrocardiogram from a twenty-two year old Negro.

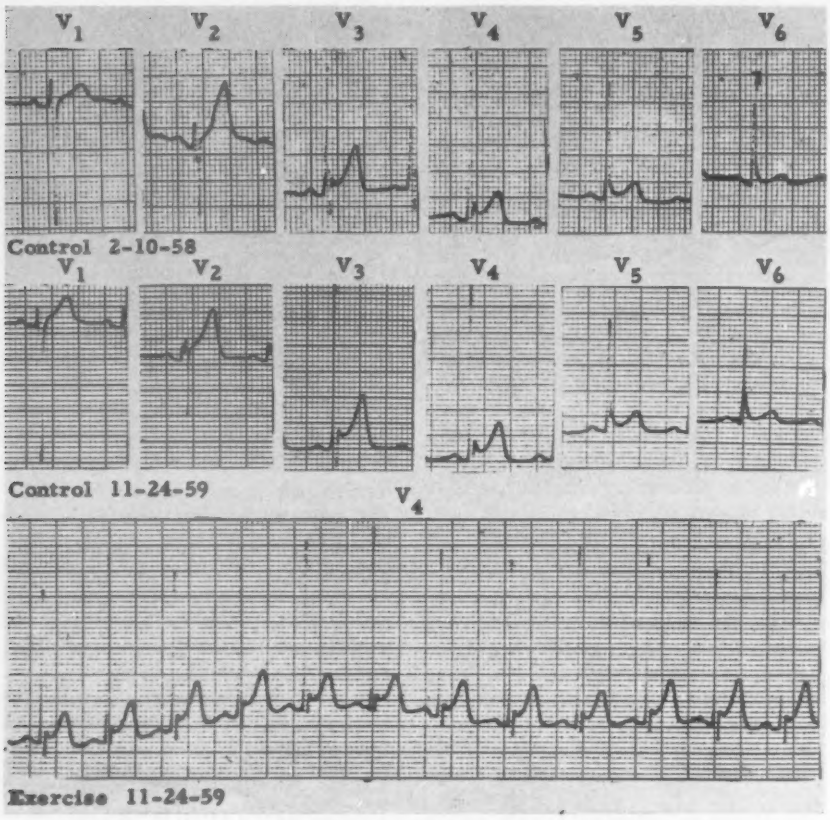

FIG. 4. *Effect of exercise.* The elevated RS-T segment variant persists following exercise. The subject was thirty-seven years old.

ten patients continued to exhibit a distinctly elevated S-T segment following exercise and indeed, in two, the segmental elevation became more apparent due to Ta wave inscription associated with the tachycardia of the exercise procedure (Fig. 4).

Hyperventilation: The effect of brief hyperventilation upon the normal RS-T segment variant was quite striking; seventeen of the twenty-seven patients completing the hyperventilation study showed marked T wave inversion in the precordial leads exhibiting the elevated RS-T segment (Fig. 5). A similar degree of precordial T wave inversion was observed following both brief hyperventilation and exercise in nine subjects (also shown in Fig. 5 and 6).

In general, the elevated RS-T segment pattern persisted, with minor variations in degree of segmental shift, over a period of many months.

ILLUSTRATIVE CASES

In an effort to show the ramifications and implications of the normal RS-T segment variant, its similarity to pericardial and myocardial electrocardiographic change is depicted by individual case presentation:

Juvenile Pattern Simulating Myocardial Injury: Electrocardiographic association of the normal RS-T segment variant with functional precordial T wave inversion, *viz.*, the "juvenile pattern" (Fig. 6). This particular pattern may mimic completely that of an acute myocardial episode presenting with injury and ischemic changes. Two previous electrocardiograms of this patient taken in 1957 were interpreted elsewhere as "subacute pericarditis."

Pericarditis: The injury phase of an acute pericarditis simulating the usual electrocardiographic criteria of "the normal RS-T segment variant." The clinical picture and serial electrocardiograms established the correct diagnosis (Fig. 7).

Acute Coronary Insufficiency: Transitory segmental precordial RS-T shift associated with acute coronary insufficiency (Fig. 8).

Asthenic Habitus: Association of the normal RS-T segment variant with an extremely asthenic habitus, suggesting residual anteroseptal wall myocardial infarction (Fig. 9). Osher

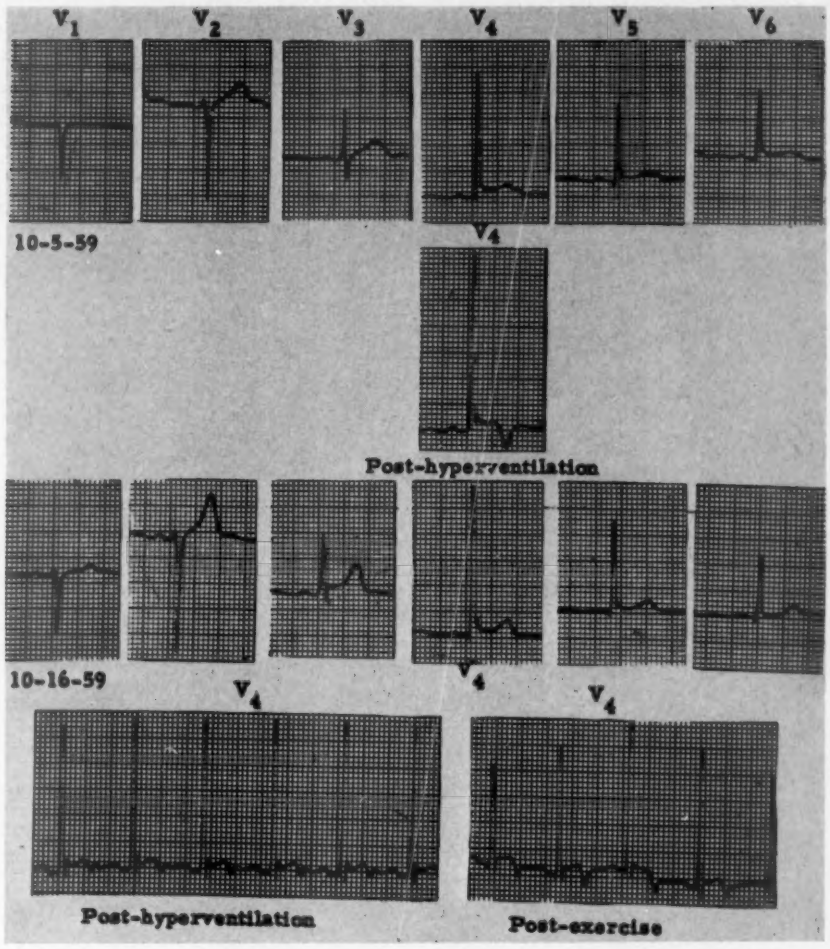

FIG. 5. *Effect of hyperventilation.* Note the marked T wave inversion in V_4 following brief hyperventilation in the tracing of October 5, 1959. Subsequently, both brief hyperventilation and exercise resulted in T wave inversion. The subject was thirty-seven years old.

and Wolff[7] and Edeiken[8] have previously described the normally elevated right and mid-precordial S-T segmental take-off from the r′ component of the QRS complex. The factor of an asthenic habitus only serves to mask the r′ component and add further difficulty in the over-all interpretation of a given electrocardiogram. Serial tracings with the precordial leads taken in the sub-prime positions are mandatory for proper electrocardiographic evaluation.

COMMENTS

Certain salient features of this interesting electrocardiographic pattern, recounted from the works of others as well as the current data, required re-emphasis and re-evaluation. This variant, although most commonly seen in the young Negro, is present in approximately 1 per cent of adult population and has a wide age distribution and degree of S-T segmental elevation. It exhibits a distinct predilection for the precordial leads V_3, V_4 and V_5 and, as shown in Figure 1, is characteristically associated with moderate degrees of counterclockwise rotation. Although it usually persists from months to years, the degree of S-T segment elevation may be variable or even transient in a given subject.[2,3,6] The segmental elevation typically has a smooth downward concavity and ends in a symmetrically limbed T wave which is often of large amplitude. The elevated segmental S-T take-off occurring with acute pericarditis is usually directed tangentially upward to the proximal summit of the T wave, without a clear-cut downward concavity.

Contrary to previous reports,[2–5] exercise did not consistently lower the elevated S-T segment of the normal variant in the current study. Chapman and Overholt[4] observed that exer-

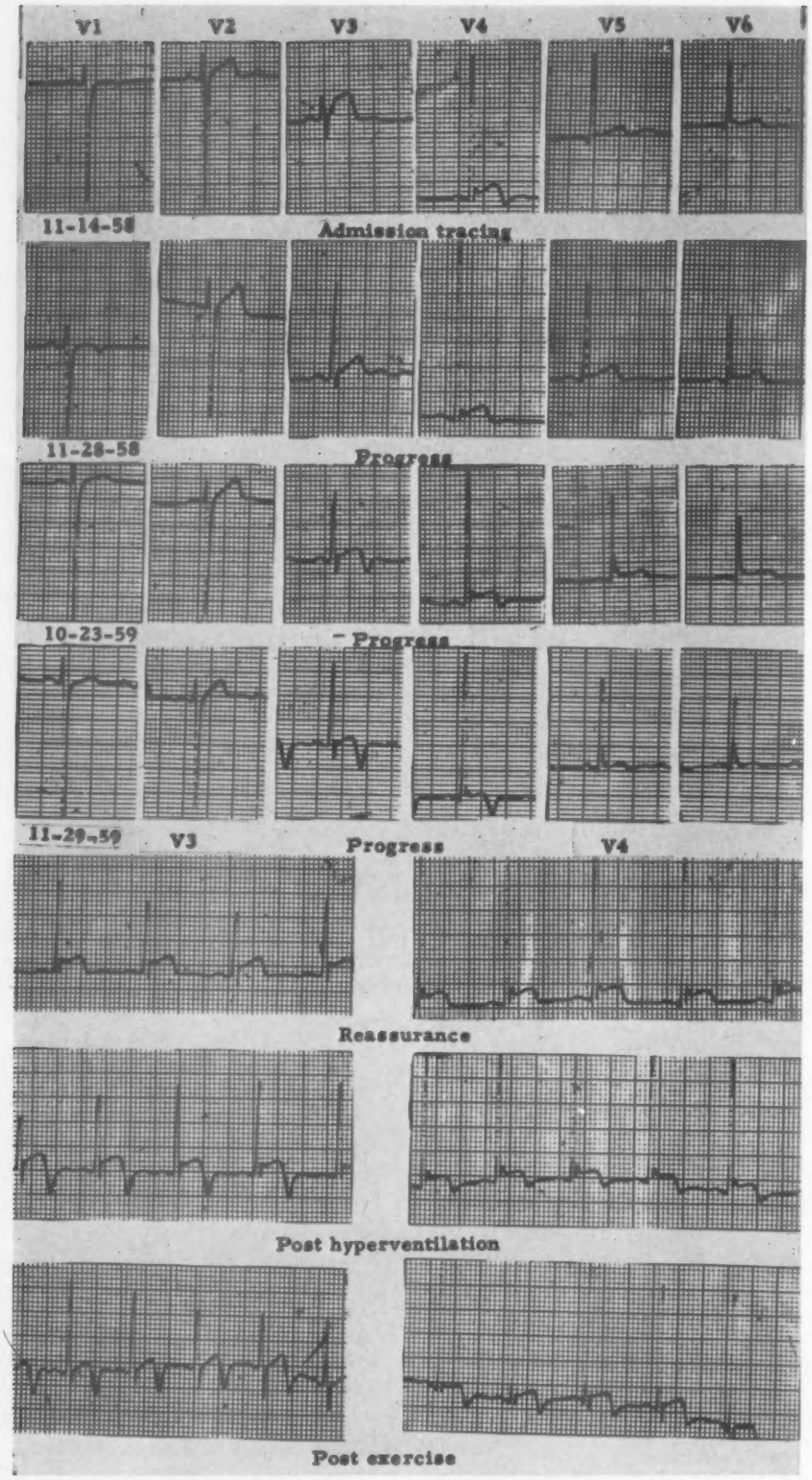

Fig. 6. *Juvenile pattern simulating myocardial injury.* The association of the RS-T segment variant with the "juvenile pattern" closely simulates the acute injury-ischemic phase of an acute myocardial episode. The original T wave changes were not present in the progress tracing of November 28, 1958, but were clearly present in the subsequent tracings one year later (October 23, 1959 and November 29, 1959). At this time, reassurance resulted in normalization of the T wave, and both hyperventilation and exercise resulted in T wave inversion in leads V_3 and V_4. The subject was a thirty-seven year old Negro.

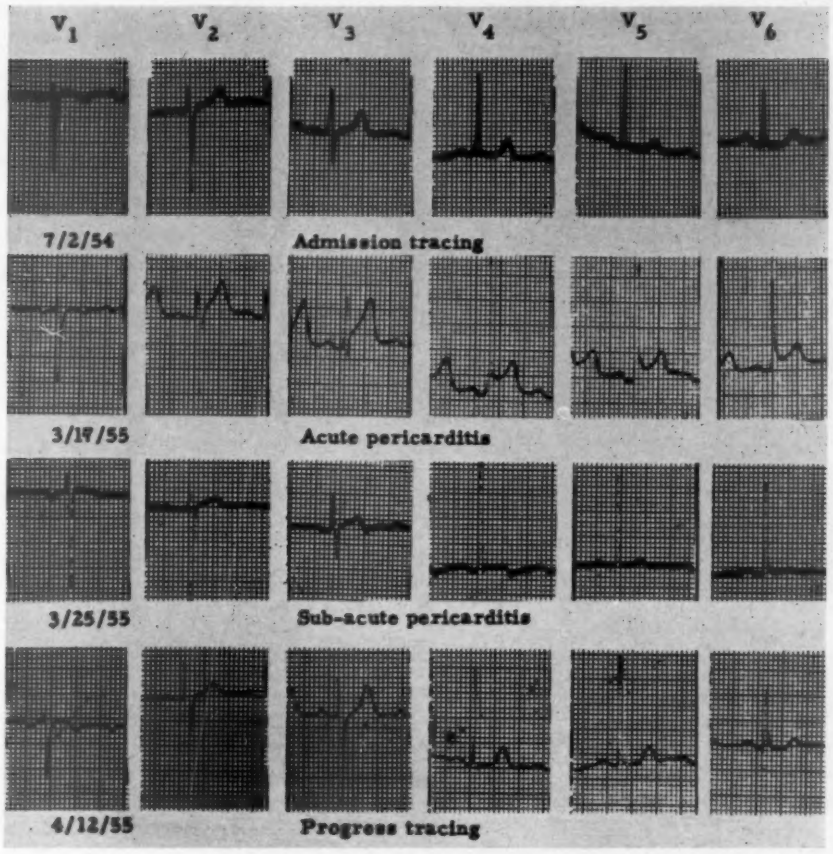

FIG. 7. *Acute pericarditis.* Elevated RS-T segments due to acute pericarditis with subsequent progression to the subacute phase and ultimate return to normal. A downward concavity of the RS-T segment is suggested in the tracing of March 17, 1955. The subject was a fifty-two year old Negro.

cise did not alter the segmental elevation of the injury potential secondary to acute benign pericarditis, whereas in all nine of their control subjects exhibiting the normal RS-T segment variant, eight of whom were Negro, exercise resulted in prompt return of the S-T elevation to the isoelectric line. The present data, seemingly, would not allow such an exact differential by the simple expedient of exercise, and reliance upon the clinical picture and serial electrocardiographic tracings is necessary.

Bedford and Thomas[9] have reported that reciprocal S-T segmental depression is not seen in lead aVR with instances of the normal S-T segment variant, whereas this finding is the rule in pericarditis. Rather, it appears that the presence or absence of reciprocal S-T segment shift is related to the degree of precordial S-T elevation, whether this is due to the normal RS-T segment variant or to an active pericarditis.

The significance of the normal RS-T segment variant has considerable clinical implication, for failure to recognize this pattern as a normal variant, even though marked in degree, may result in irreversible iatrogenic heart disease with all its attendant economic and social repercussions. This is particularly true if this variant is associated with the "juvenile pattern," *viz.*, functional T wave inversion in the mid- and left precordial leads. Here one finds not only elevated S-T segments but also gross T wave inversion, simulating the acute injury-ischemic phase of an acute myocardial episode or subacute pericarditis. This is brought into sharper focus when one recalls that brief hyperventilation (ten to fifteen seconds) resulted in marked precordial T wave inversion in seventeen of the twenty-seven patients currently studied. Exercise resulted in T wave inversion in nine patients entirely similar to that seen following brief hyperventilation. These findings require a fresh approach to the interpretation of the various exercise tolerance tests in the presence

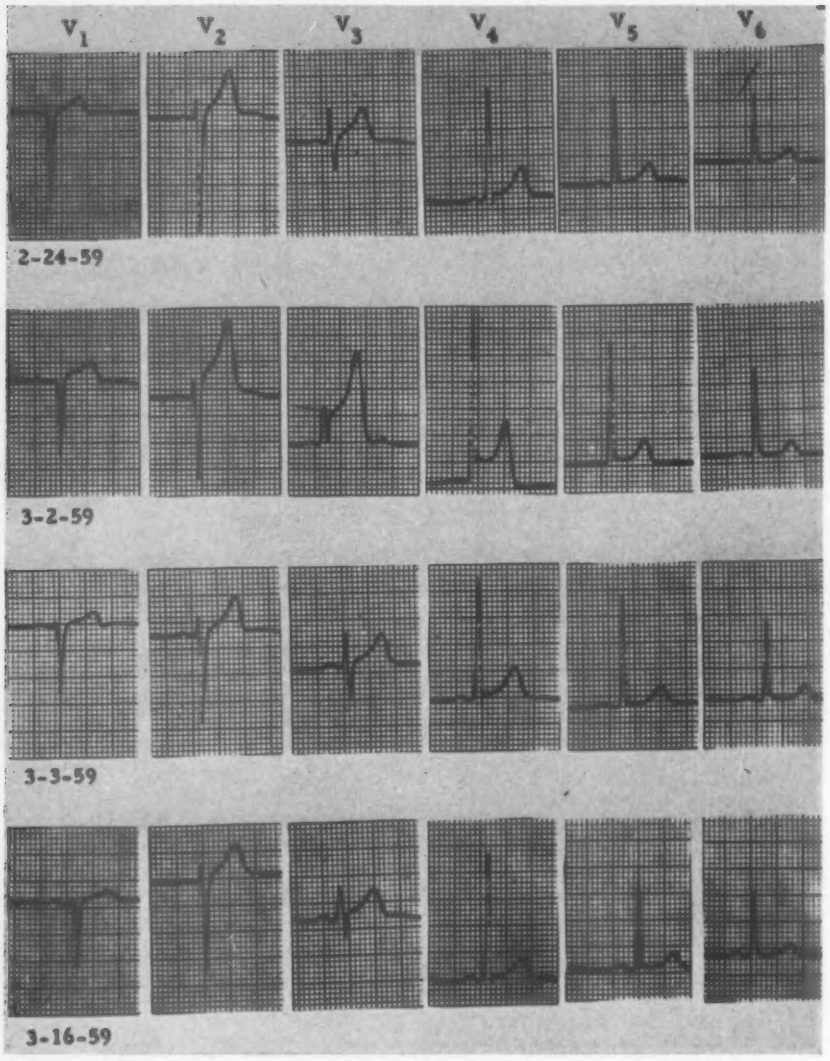

FIG. 8. *Acute coronary insufficiency.* Transitory elevation of the precordial RS-T segments in V_2, V_3 and V_4, associated with acute coronary insufficiency (March 2, 1959). This fifty-one year old patient subsequently had a positive exercise tolerance test with depression of the RS-T segments in leads V_3, V_4 and V_5.

of the normal RS-T segment variant, as hyperventilation is an inherent factor in any exercise procedure.

In our initial description[10] of the "juvenile pattern," an isoelectric S-T segment was required for inclusion. The current data suggest that the "normal RS-T segment variant" and the "juvenile pattern" are intimately allied, in that both patterns are extremely susceptible to marked T wave inversion following brief hyperventilation. Grusin[11] previously noted this relationship in a study of South African natives, but at that time, he could not exclude the possible underlying factor of a nutritional disorder. Greene and Kelly[12] have recently suggested that malnutrition was also the provocative factor in our original series of functional T wave changes in the Negro. This premise was based on their failure to find a single instance of an inverted T wave beyond V_2 in an electrocardiographic survey of 144 adult Negro hospital employees. This variance in data does not mean that precordial T wave inversion does not occur in the normal adult Negro. Rather, if one is to appreciate the wide range of normal precordial S-T segment and T wave changes, one should include a survey on hospitalized patients, for here emotional tensions and anxieties are paramount and the electrocardiographic changes of hyperventilation are readily expressed.[13,14] One need not construe the factor of hospitalization as an index of

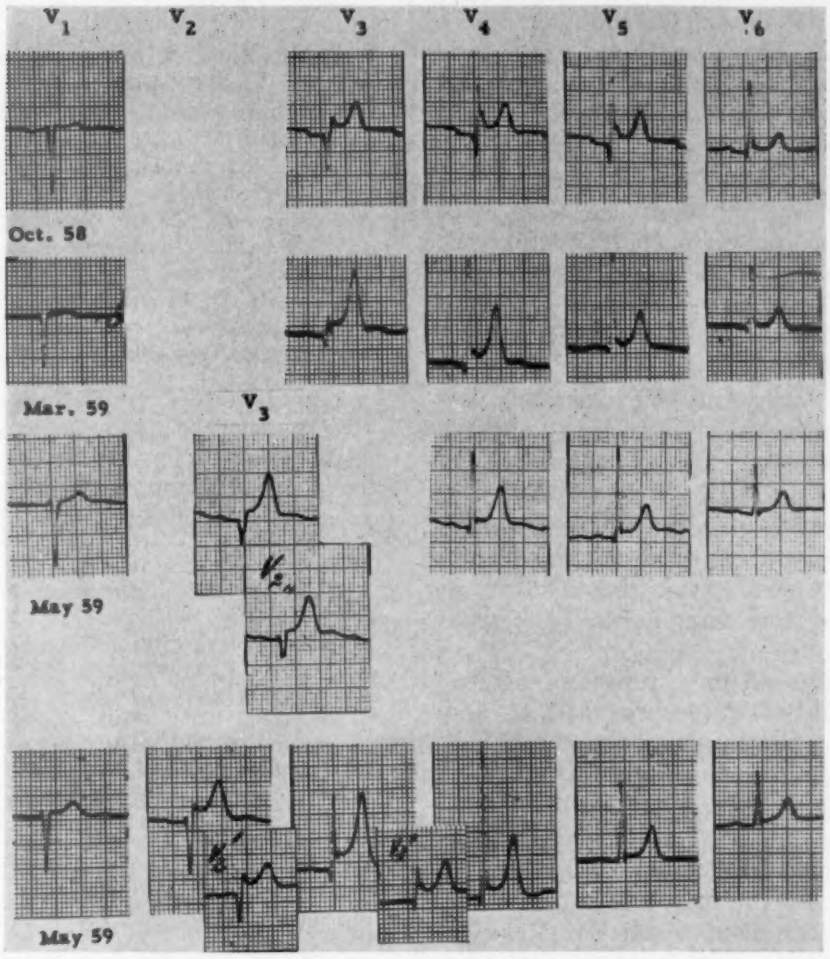

FIG. 9. *Asthenic habitus.* The tracing of March 1959 was interpreted elsewhere as residual anteroseptal wall myocardial infarction. An earlier tracing however of October 1958 showed similar changes as did the progress tracing of May 1959. By placement of the exploring chest electrode two interspaces lower than conventional, necessitated by the asthenic body habitus, a distinct rSr′ pattern was seen in V_2, with elevated RS-T segments in V_3 and V_4. The inserts V_2' and V_3' shown on the lower strip, taken one interspace higher than conventional electrode placement, were entirely similar to those of V_3 and V_4 on the initial tracing of October 1958. The patient, although seventy years of age, denied all cardiovascular symptoms and leads an extremely active existence.

cardiac disease for, apparently, it is the anxiety-provoking mechanism of hospitalization which provides the key to the "juvenile pattern."

Goldman[15] has recently published electrocardiographic data on five patients presenting with functional precordial T wave inversion, four of whom also exhibited the normal RS-T segment variant. The clinical implications were evident, as one patient had previously been diagnosed as having had a myocardial infarction, and another was subjected to thoracotomy for relief of suspected pericardial disease. All electrocardiographic patterns were subsequently interpreted as normal variants.

SUMMARY AND CONCLUSIONS

The normal precordial RS-T segment variant presents in one of two rather distinct electrocardiographic patterns. It is most frequently seen in precordial leads V_3, V_4 and V_5, and is associated with variable degrees of counterclockwise rotation.

This elevated S-T segment arises from a distinct notch or slur on the distal QRS complex, characteristically has a downward curve or concavity, and terminates in a symmetrically limbed T wave which is often of large amplitude.

Although it occurs in approximately 1 per

cent of an adult population, it is most commonly seen in the young Negro adult and has a wide age distribution. The degree of segmental elevation usually persists as a relatively fixed pattern over a period of years.

Contrary to previous reports, exercise did not uniformly lower the normal S-T segment variant to isoelectric, and consequently, this procedure does not appear to be of value in excluding an active pericarditis.

Brief hyperventilation (ten to fifteen seconds) resulted in gross precordial T wave inversion in seventeen of the twenty-seven patients presenting with the normal S-T variant.

Exercise and hyperventilation resulted in entirely similar precordial T wave inversion in nine of the twenty-four patients so studied. This requires a fresh approach to the interpretation of the various exercise tolerance tests in the presence of the normal RS-T segment variant.

The association of the "juvenile pattern" and the normal RS-T segment variant may completely mimic the electrocardiographic findings of an injury-ischemic pattern of an acute coronary episode.

The injury potential of an acute pericarditis or an acute myocardial episode may on occasion simulate the normal S-T segment variant. The clinical picture and serial electrocardiograms should establish the correct diagnosis.

Acknowledgment

We extend our appreciation to John K. Curtis, M.D. for review of this manuscript, to Mrs. Donna Klevgaard for technical assistance, and to Mrs. Lila Mulloy for secretarial preparation. The photographic reproductions were compiled by Mr. Forrest J. Fischer, Department of Medical Illustration, Veterans Administration Hospital, Madison, Wisconsin.

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Idiopathic Atrial Fibrillation*

HENRY N. NEUFELD, M.D., F.A.C.C., CORNELIUS A. WAGENVOORT, M.D., HOWARD B. BURCHELL, M.D. *and* JESSE E. EDWARDS, M.D.

Rochester, Minnesota

THE OCCURRENCE of atrial fibrillation usually means that underlying cardiac disease of some type is present. The most common cause of atrial fibrillation is mitral valvular disease. Other causes are coronary atherosclerosis, hypertensive disease, thyrotoxicosis, constrictive pericarditis and certain congenital malformations of the heart. In isolated instances, however, atrial fibrillation occurs in hearts that have little or no anatomic evidence of pre-existing disease. Gossage and Hicks,[1] in 1913, first described cases in which atrial fibrillation occurred in patients with no other clinical evidence of heart disease. No underlying organic cardiac disease was found on pathologic examination in one of their cases. Since that time many series have been published, and the condition has been described as benign, idiopathic, functional or simply fibrillation of unknown origin without heart disease.[2–6] Some authors have reported cases in which the patients were older than sixty and seventy years; however, no pathologic examination was made in these cases.

The underlying mechanism of idiopathic atrial fibrillation is not known. Phillips and Levine[2] suggested that atrial fibrillation of this type could be the result of a trigger phenomenon of neurogenic origin in certain patients who are susceptible to functional nervous instability but are otherwise within normal limits. Pathologic studies have been made by Frothingham[7] and Yater;[8] their impression was that the heart did not reveal any characteristic lesions.

Considered clinically, idiopathic atrial fibrillation has been thought to result in cardiac dilatation or progressive congestive failure or both.

The purpose of this paper is to describe five cases of idiopathic atrial fibrillation, in which evaluation included clinical, electrocardiographic and necropsy study.

REVIEW OF CASES

The material for this study was selected from twelve cases studied at necropsy at the Mayo Clinic in the years 1950 to 1959 inclusive, in which permanent atrial fibrillation had been unexplained clinically. Of these twelve cases, seven were excluded because pathologic evidence of moderate to severe coronary atherosclerosis was present. In four of the seven cases exclusion was made primarily on the basis of gross examination; in the three others histologic examination revealed significant coronary atherosclerosis. One of the patients with coronary atherosclerosis had manifested cor pulmonale. In the remaining five cases the atrial fibrillation was unexplained.

CLINICAL FEATURES

No pathologic evidence of endocarditis, myocarditis, pericarditis or amyloidosis was found in any of the five cases. In no case was hypertension known to have been present (although this possibility had to be given due consideration in view of the somewhat increased heart weights that were found). There was no record of hyperthyroidism, the presence of a goiter or thyroidectomy. The clinical features in each of the five cases were similar. The most pertinent features, together with data on age and sex, are summarized in Table 1.

No symptoms heralded the onset of atrial fibrillation. Ultimately, congestive cardiac failure became apparent in two patients. In one of these (Case 5), failure occurred eight years before death, at the time the irregularity was first noted. In the other patient (Case 1), congestive cardiac failure appeared a few months prior to death and fourteen years after atrial fibrillation was first observed.

* From the Sections of Pathological Anatomy and Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minnesota. This investigation was supported in part by a research grant (No. H-4014) from the National Heart Institute, U. S. Public Health Service.

TABLE 1
Clinical Data in Five Cases of Idiopathic Atrial Fibrillation*

Case	Sex	Age (yr.) When Fibrillation Was Recognized†	Interval between Diagnosis of Fibrillation and Death	Cardiomegaly	Congestive Heart Failure	Blood Pressure (mm. Hg)	Cause of Death	Heart Weight (gm.)
1	M	61	14 yr.	+	+	135/70	Congestive heart failure	505
2	M	57	2 yr.	+	−	140/85	Cerebral infarction	405
3	M	47	5 wk.	+	−	125/80	Multiple systemic emboli	525
4	M	66	9 mo.	−	−	135/75	Sudden death after exploratory laparotomy	455
5	F	77	8 yr.	++	++	130/90	Cerebral infarction	455

* No evidence of hypertension or thyrotoxicosis was found in any patient.
† The age at the onset of fibrillation was not known in any case.

When multiple observations were made, atrial fibrillation was observed on each examination, the period of observation varying from five weeks to fourteen years. In two patients soft systolic murmurs were noted. Cardiomegaly was noted clinically in four patients throughout the period of observation.

Electrocardiographically, atrial fibrillation was present in all cases. No significant abnormalities in the QRS or T complexes were observed on multiple electrocardiograms. In two cases prominent F waves were noted. The incidence of high voltage F waves was not different from that noted in patients with associated heart disease.

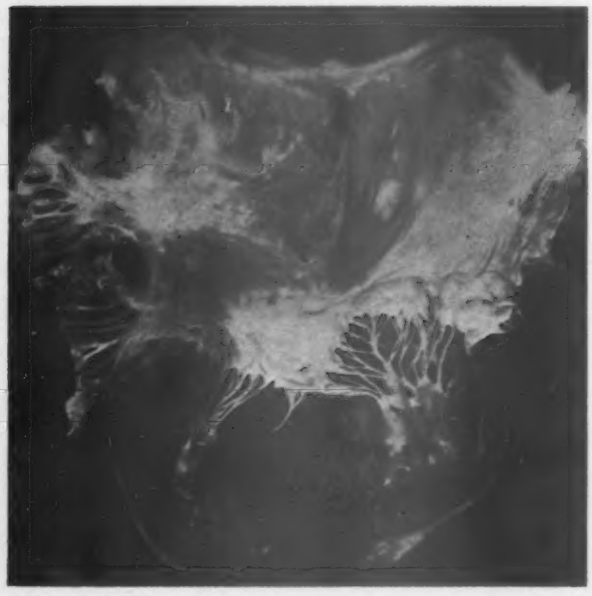

FIG. 1. Case 1. Left side of heart, showing prominent dilatation of left atrium. Endocardium of this chamber is gray, indicating endocardial fibrous thickening. Mitral valve is within normal limits. Left ventricle shows moderate hypertrophy of wall and possibly slight enlargement of chamber.

PATHOLOGIC FEATURES

Necropsy was performed in each case. The heart was studied grossly and histologically, and histologic preparations of the other organs were also available for study. In no case were significant pathologic changes found in the thyroid gland or the kidneys, giving support to the clinical impression that no thyrotoxic or hypertensive disease had been present. The myocardium was unremarkable histologically, except for a small localized scar in one case. The coronary arteries showed only minimal and insignificant degrees of atherosclerosis in scattered foci. No valvular disease was present in any case.

Heart weights were somewhat greater than the normal in each case, varying from 405 to 525 gm. Left atrial enlargement of moderate to pronounced degree characterized each case. Right atrial enlargement was likewise present in each case but to less striking degrees. In all cases one or both of the ventricles showed some degree of hypertrophy. The endocardium of the left atrium was greatly thickened in all cases, measuring as much as 2,000 μ in some regions. No significant changes were found in the pulmonary vessels. Figures 1 to 4 demonstrate the characteristic findings in this series of cases.

Intracardiac thrombosis was demonstrated at

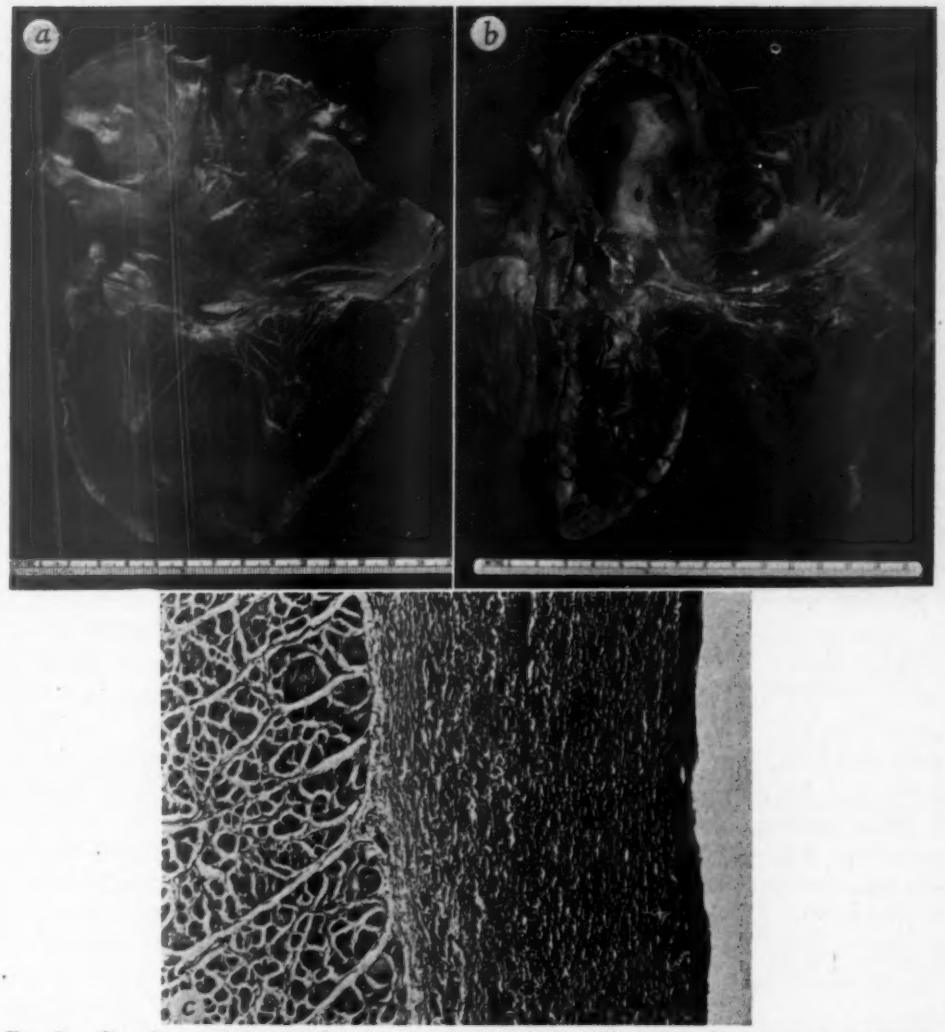

FIG. 2. Case 2. A, left side of heart, showing moderate dilatation of left atrium. Mitral valve is within normal limits. Left ventricular wall is mildly hypertrophied. B, right side of heart, showing moderate dilatation of right atrium. Tricuspid valve is within normal limits. Right ventricular wall is moderately hypertrophied. C, thickened endocardium of left atrium (elastic-tissue stain counterstained with van Gieson's stain; reduced from × 100).

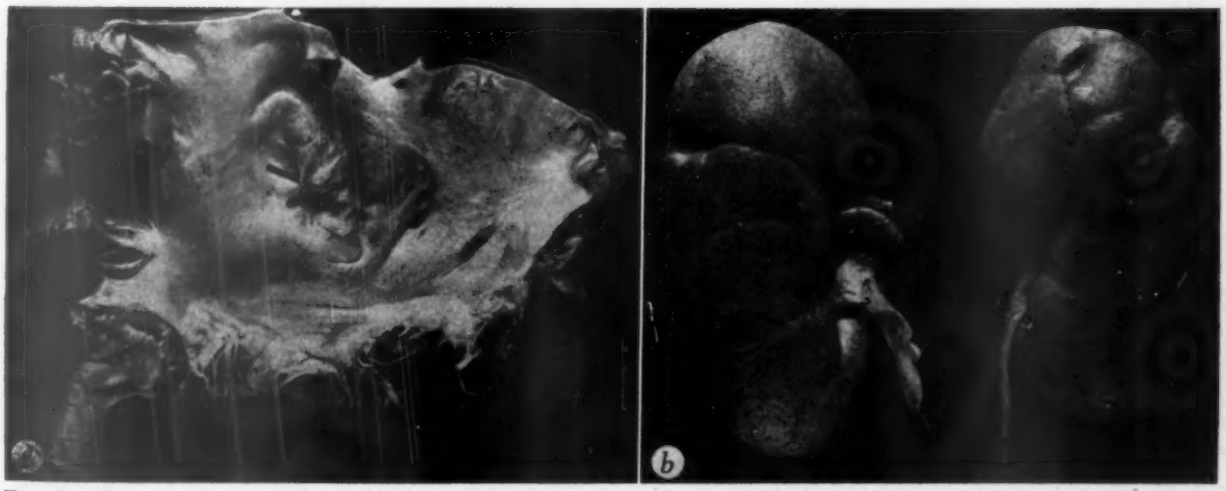

FIG. 3. Case 3. A, left atrium, showing enlargement of chamber and fibrous thickening of endocardium. Mural thrombus is attached to wall of atrial appendage. Patent foramen ovale is seen. The mitral valve is within normal limits. B, kidneys demonstrate focal scars of infarcts that resulted from emboli derived from left atrial thrombus.

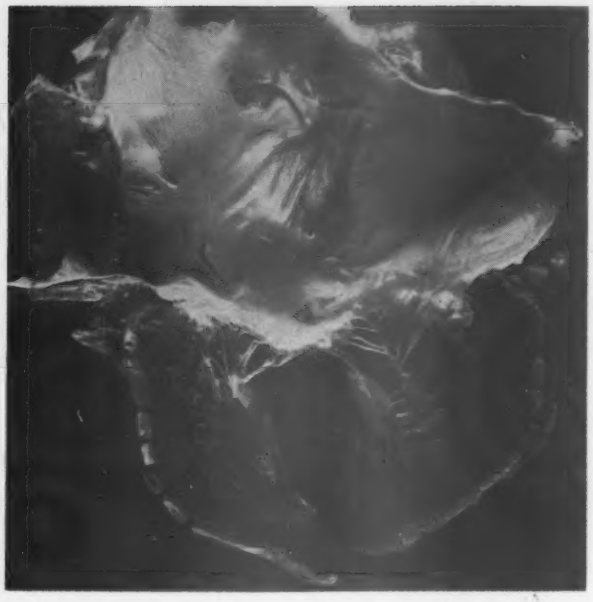

FIG. 4. Case 5. Left side of heart, showing prominent enlargement of left atrium. Mitral valve is within normal limits. Left ventricular wall is hypertrophied.

necropsy in only one case, that of a 47 year old man (Case 3, Fig. 3); the site of the thrombosis was the left atrial appendage. In this case peripheral embolism had occurred, requiring amputation of a leg. It was the arterial occlusion that first brought to light this patient's arrhythmia. In this case and in one other (Case 1), the cause of death was believed to be related to the fibrillation.

In two patients (Cases 2 and 5), cerebral infarction was demonstrated at necropsy, but no intracardiac or cerebrovascular basis for the infarction could be found. It is possible that intracardiac thrombi had been present and had left the heart in their entirety to form cerebral emboli, but this explanation is hypothetical.

COMMENT

From the history of patients with idiopathic atrial fibrillation, it is often difficult to establish the arrhythmia as being truly idiopathic or to determine its exact time of onset; this was the experience in the cases presented herein and has generally been the experience of others. The reason for this difficulty is that this form of atrial fibrillation is well tolerated and usually does not cause any discomfort for the patient. When the disorder is discovered in an early stage, the finding is usually fortuitous. As mentioned, there was no evidence of hypertension or thyrotoxicosis in the present series of cases; in addition, none of the patients was alcoholic or indigent, so that malnutrition was not a likely cause of the arrhythmia.

Anatomically, the first change after the onset of atrial fibrillation is probably progressive enlargement of the left atrium. This change occurred in all five cases and was associated with a certain degree of enlargement of the right atrium and hypertrophy of one or both ventricles. The endocardial thickening of the left atrium was probably a reaction to the stretching of the endocardium incident to enlargement of the atrial chamber. The absence of pulmonary vascular changes suggests that the right atrial enlargement was not the result of right ventricular failure due to pulmonary hypertension.

The cause of death of two patients in the present series was believed to be related to chronic atrial fibrillation. One of these (Case 3) had multiple systemic emboli to the leg, kidneys and left occipital lobe. The other (Case 1) died in severe congestive failure; this patient had cardiomegaly without any other findings except chronic atrial fibrillation. Two patients (Cases 2 and 5) had massive infarction of the brain, but no embolus could be found. In the last patient (Case 4), there was no direct connection between death and the chronic atrial fibrillation; this patient died after exploratory laparotomy for suspected cancer of the pancreas.

The incidence of thrombi and systemic embolization in idiopathic atrial fibrillation is a controversial subject. Phillips and Levine[2] studied eighty-four cases and found no clinical evidence of embolism. No intracardiac thrombi were found in any of their cases studied at necropsy. The absence of thrombi and peripheral embolization was also noted by Evans and Swann.[3] Weintraub and Sprecace,[9] on the other hand, described a case of idiopathic atrial fibrillation complicated by cerebral embolism. In one patient of this series (Case 3), thrombi were found in the left atrium, and this patient had peripheral emboli as well. In none of the other four patients were thrombi found in the heart on gross or histologic examination. Cerebral embolism may have been present in two patients (Cases 2 and 5).

As far as cardiac function and hemodynamics are concerned, no studies are available in cases of idiopathic atrial fibrillation. It is generally assumed that the absence of effective contraction in atrial fibrillation is important in reducing the ventricular diastolic filling. Hemodynamic data[10–12] are available from patients with underlying heart disease and chronic atrial fibrillation

before and after restoration of normal sinus rhythm with quinidine. These data are not uniform, but generally they indicate that a significant rise in cardiac output occurs when sinus rhythm is restored.

The incidence of idiopathic atrial fibrillation is unknown; the arrhythmia may occur more often than can be established. Those patients with idiopathic atrial fibrillation who are seen at necropsy are in the higher age groups. Since this condition can be benign for many years, some persons with idiopathic atrial fibrillation may, when they reach the older age groups, experience coronary atherosclerosis with or without hypertension and have the fibrillation explained on the basis of the recognized heart disease, whereas, in fact, the arrhythmia preceded it.

Clinically, the baneful effect of atrial fibrillation is suggested in our group of cases and in observations of others; the arrhythmia may in itself be a contributing cause of congestive heart failure. In support of this possibility is the fact that some patients with idiopathic atrial fibrillation show pronounced clinical improvement after sinus rhythm is restored.[2]

It should be emphasized, on the other hand, that about 10,000 necropsies were reviewed and only five cases of this disorder were found. The question arises why more cases of failure due to idiopathic atrial fibrillation do not occur, since this condition is not rare in the older age groups.

Summary

The records of five patients with idiopathic atrial fibrillation were reviewed. These cases were selected on the basis of the absence of any heart disease or other condition that might have accounted for the arrhythmia. No significant changes were present in the coronary arteries in any of the cases. No symptoms marked the onset of the fibrillation.

Anatomically, the weight of the heart was greater than normal in all five cases. Left atrial enlargement and endocardial thickening were also present in all cases. Intracardiac thrombosis was noted in only one case and was associated with multiple peripheral emboli.

In two cases the cause of death was thought to be related to the chronic atrial fibrillation. It is suggested that idiopathic atrial fibrillation may go unrecognized in some persons until later life, when some form of heart disease develops that is then taken to be the cause of the arrhythmia.

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Atrial Septal Defect in Older Age Groups

With Especial Reference to Atypical Clinical and Electrocardiographic Manifestations*

LEONARD S. SOMMER, M.D. *and* IGNATIOS J. VOUDOUKIS, M.D.

Miami, Florida

ATRIAL SEPTAL defect is the most common congenital cardiac malformation in middle-aged patients.[1,2] It may be compatible with long life and may actually be an incidental finding at postmortem examination.[3] The clinical picture of this disorder is well recognized in children and young adults. In the middle-aged or elderly patients, however, the clinical profile may be bizarre and may suggest acquired or degenerative heart disease or primary pulmonary disease.

The purpose of this communication is to contrast ten such instances of clinically atypical atrial septal defect, masquerading as other forms of cardiopulmonary disorder.

MATERIAL

Ten patients, exhibiting atypical clinical or electrocardiographic findings, were proved to have an atrial septal defect. Their ages ranged from forty-two to seventy years. The diagnosis was confirmed by finding a significant step-up of blood oxygen content at the right atrial level in each and passage of a catheter across the atrial septum during venous catheterization in seven. The two patients operated upon were found to have secundum-type defects; one of these was further confirmed at postmortem examination.

OBSERVATIONS

Clinical Profile: In eight patients the age at onset of symptoms varied from forty to sixty-two years. In one, complaints appeared in childhood and in another at age twenty years. The average age at which symptoms began was thirty-nine years. The presenting symptoms were those of right heart failure and dyspnea in four patients, syncopal attacks in two and palpitations in two. In two women chest pain occurred as the initial symptom, in each at the age of forty-two years. One of these was still menstruating and had no stigmata of hypertension or diabetes mellitus. The other woman was mildly hypertensive. Of the five female patients systemic hypertension was present in three. Two of the five male patients had associated pulmonary disorders.

Physical Signs: Anterior chest deformity was present in only two patients and was slight in degree. The cardiac impulse was most prominent in the region of the left axillary line or was palpable both here and parasternally in five patients. In the other five the impulse was localized to the left sternal border.

The second heart sound in the pulmonary area was split in all but one patient, widely in seven and narrowly in two. P_2 was accentuated in all instances. The first sound was accentuated in three individuals and split in four. A rather harsh grade 2 to 4 systolic murmur, associated with a thrill in three instances, was present in all, best heard in the second or third left intercostal space near the sternal border. It was transmitted downward and in a few instances toward the apex. In one patient, who had significant left atrial enlargement, a widely split second heart sound simulated an opening snap of mitral stenosis.

Electrocardiographic Patterns: Complete left bundle branch block was present in one patient (Case 2, Table 1 and Fig. 1). Another subject with evidence of a probable old apical infarction showed an intraventricular conduction defect (Case 5, Fig. 2). Complete right bundle branch block was noted in five patients. In-

* From the Division of Cardiovascular Disease, Department of Medicine, University of Miami School of Medicine and the Cardiac Clinic and Cardio-Pulmonary Laboratory, Jackson Memorial Hospital. Supported by grants from the Heart Association of Greater Miami and the National Heart Institute.

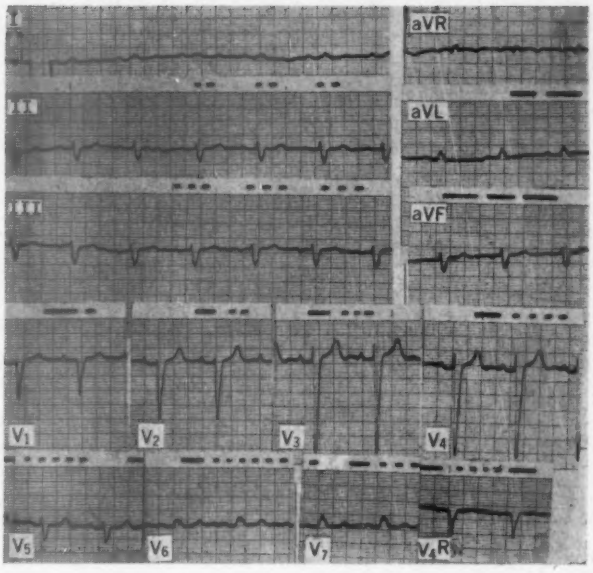

FIG. 1. Case 2. Electrocardiogram. Left bundle branch block. Previous tracings revealed atrial flutter.

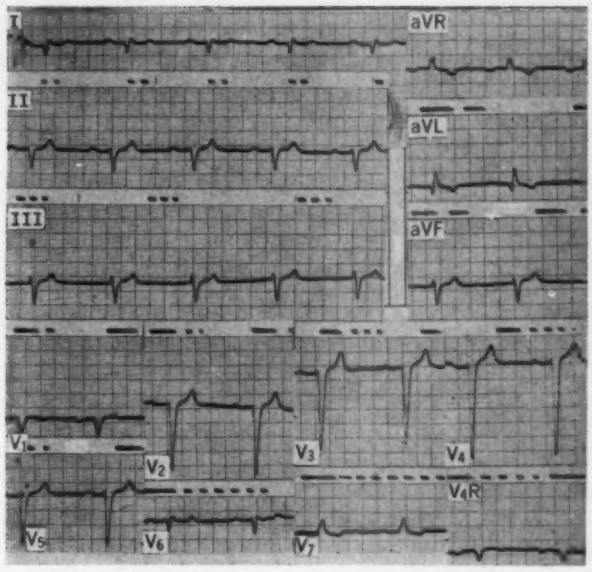

FIG. 2. Case 5. Electrocardiogram. Intraventricular conduction defect; probably old apical infarction.

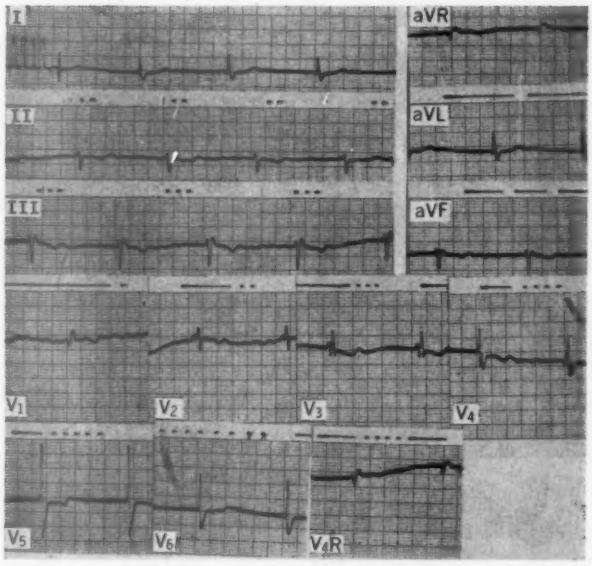

FIG. 3. Case 4. Electrocardiogram. Atrial fibrillation, complete heart block, right bundle branch block; probably left ventricular hypertrophy.

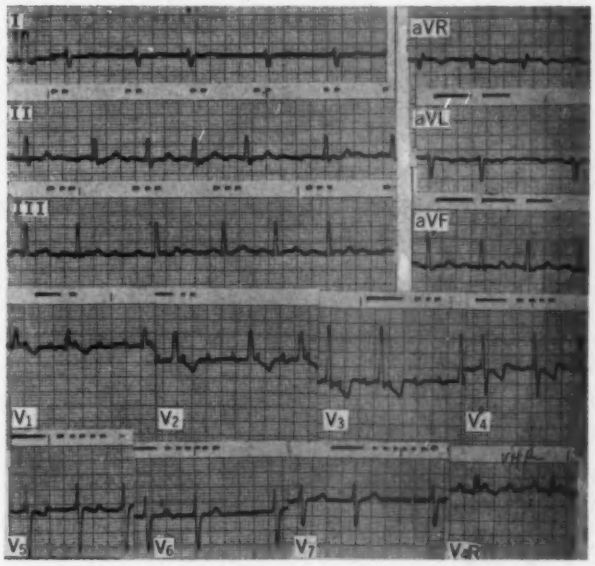

FIG. 4. Case 8. Electrocardiogram. Atrial tachycardia with varying block, right bundle branch block.

complete right bundle branch block was found in only two patients (Cases 7 and 9) and right ventricular hypertrophy in one (Case 10). In addition, complete heart block (Case 4, Fig. 3) and a variety of supraventricular arrhythmias were seen including atrial fibrillation, atrial flutter and atrial tachycardia with varying block (Case 8, Fig. 4, Table 1).

Fluoroscopic and Radiographic Features: There was moderate to marked cardiomegaly in all but one instance. The aorta was relatively inconspicuous in seven and the arch showed atherosclerotic calcification in two. The pulmonary conus segment was prominent in all cases. The pulmonary arteries were markedly enlarged and the peripheral vascular markings were increased, with slight to moderate increase in intrinsic pulsations, in eight patients. The left atrium was enlarged in three individuals, one with complete heart block, another with persistent atrial fibrillation, and a third with atrial tachycardia with varying block; these were also the patients with the largest overall heart size. Right atrial and right ventricular

TABLE I
Electrocardiographic Data

Case No.	Rhythm	Conduction	Hypertrophy
1	Wandering pacemaker	RBBB	LAH
2	Intermittent atrial flutter and fibrillation	LBBB	...
3	Atrial fibrillation	RBBB	...
4	Atrial fibrillation	RBBB Complete A-V block	LVH?
5	Paroxysmal atrial fibrillation	IVCD	LAH
6	Intermittent atrial flutter and fibrillation	RBBB	CAH
7	Normal sinus	IRBBB	...
8	Atrial fibrillation, sinus rhythm and paroxysmal atrial tachycardia	Varying A-V block, RBBB	...
9	Normal sinus	IRBBB	LAH
10	Normal sinus	Normal	RAH, RVH

NOTE: RBBB = right bundle branch block; IRBBB = incomplete right bundle branch block; LBBB = left bundle branch block; RAH = right atrial hypertrophy; LAH = left atrial hypertrophy; CAH = combined atrial hypertrophy; LVH = left ventricular hypertrophy; and IVCD = intraventricular conduction defect.

enlargement, and normal left ventricular size, were noted in all but one instance, the patient with the normal transverse cardiac diameter (Case 2).

Hemodynamic Data: All ten patients were studied by venous cardiac catheterization (Table II), and showed a significant increase in the oxygen content of right atrial blood; in addition, a catheter was successfully passed across an atrial septal defect in seven. There was slight pulmonary hypertension in five patients, moderate in two, and severe in one; one had normal pulmonary arterial pressure; in one, the pulmonary artery could not be entered, but right ventricular systolic pressure was moderately elevated. Those with normal or slightly elevated pulmonary arterial pressures had large left to right shunts. Two patients with increased pulmonary vascular resistance had relatively small left to right shunts. The arterial oxygen saturation in seven patients was slightly reduced, ranging from 80 to 90 per cent, probably due to small right to left shunts.

Results of Surgery: In two women (Cases 7 and 10) the atrial septal defect was closed by direct suture technic under hypothermia. One of these (Case 10), aged forty-two years, died within hours after surgery and at autopsy revealed an old anteroseptal myocardial infarction with mural thrombus, and severe atherosclerosis of the anterior descending coronary artery; the atrial defect was only partially closed. In the second patient (Case 7), aged fifty years, a probable acute myocardial infarction developed complicated by pulmonary infarction two months following uneventful surgery. Postoperatively, she had noted marked improvement in her dyspnea and had gained 15 pounds in weight. However, she has had several infrequent episodes of coronary insufficiency confirmed by electrocardiographic evidence of subendocardial ischemia of the left ventricle. Catheterization studies two years following surgery (Table II) revealed return of pulmonary artery pressure to normal and only questionable evidence of a minimal residual shunt.

COMMENTS

There is a striking difference in the clinical picture of atrial septal defect in middle-aged and elderly patients as contrasted with children and young adults. In our series 80 per cent of the patients were asymptomatic until at least the fourth decade of life. Unlike the case in young subjects with this condition, fatigue was not a prominent complaint. In all patients complications or associated diseases were present, such as arrhythmias, hypertension of the pulmonary or systemic arterial bed, coronary artery disease or pulmonary disease. This suggests that the atrial septal defect itself was well tolerated until the development of associated disorders. It is conceivable that in some patients the favorable climate in southern Florida may have been an important factor in delaying the onset of symptoms. In contrast to the fre-

TABLE II
Hemodynamic Data

Case No.	Age	Blood Oxygen Content (vol. %)				Pulmonary Arterial Pressure (mm. Hg)		Pulmonary Arterial Resistance (dynes sec. cm. $^{-5}$)	Arterial O_2 Saturation (%)		Passage of Catheter through Defect
		SVC	RA	RV	PA	S/D	Mean		Rest	After 100% O_2	
1	70	8.1	12.1	11.8	12.2	38/17	22	130	86	...	...
2	67	9.4(9.7)*	14.6(14.6)*	15.9(15.3)*	15.3	62/26	37	540	88	101	Yes
3	59	10.9	15.8	15.9	15.5	57/18	27	110	88	103	Yes
4	58	8.1	10.3	10.9	10.6	65/14	26	Normal	91	105	...
5	58	11.7	15.9	15.9	16.5	30/11	16	Reduced	97	109	Yes
6	50	13.2	15.9	16.9	16.9	105/31	47	325	86	99	Yes
7	50	9.4(10.0)†	14.9(12.3)†	15.3(11.4)†	15.2(11.7)†	47/14	27	130	94	105	S
8	43	11.1	17.8	18.2	...	78/5 (RV)	...	...	90	99	Yes
9	42	12.6	15.9	16.0	15.7	68/26	36	400	80	98	Yes
10	42	9.4	14.9	15.3	15.2	42/12	22	100	94	109	Yes, S, A

* Repeat catheterization data two years after first study.
† Two years postoperative catheterization. Dye dilution curves showed no evidence of shunt in either direction. RV = right ventricle (pulmonary artery could not be entered); S/D = systolic/diastolic; S = confirmed at surgery; and A = confirmed at autopsy.

quency and apparent benignity of atypical chest pain in young patients with atrial septal defect, in this age group chest pain may well be related to coronary artery disease.

Cardiomegaly with lateral displacement of the cardiac impulse may suggest left ventricular hypertrophy and thus lead to an erroneous diagnosis of hypertensive or valvular heart disease. However, the presence of a systolic murmur at the second or third left intercostal space with a rather widely split P_2 and an associated prominent parasternal impulse should direct attention toward the possibility of an atrial septal defect.

In children and young adults with atrial septal defect the electrocardiogram usually shows right ventricular hypertrophy or an incomplete right bundle branch block pattern.[4] This was uncommon in our series. Various atypical patterns were found, such as complete right bundle branch block and complete left bundle branch block, the latter to our knowledge hitherto not reported in the literature. Certain arrhythmias such as atrial fibrillation and flutter are not uncommon in this congenital defect. In addition, tachycardia with varying block unrelated to digitalis therapy, and complete heart block, were seen in our group. It is of interest that in one of two patients with atrial fibrillation and left atrial enlargement, direct passage of a catheter across the mitral valve excluded the presence of associated mitral stenosis.

The fluoroscopic and radiographic features must be considered as the hallmark of this congenital lesion, especially when the patient is first seen after the fourth decade of life. The striking hilar hypervascularity with a prominent pulmonary conus, enlarged pulmonary arteries and "hilar dance" at fluoroscopy, with a relatively small aorta, are always found in this condition. Left atrial enlargement may occasionally be seen in patients with marked cardiomegaly and is not related to associated mitral disease.

Cardiac catheterization, with passage of a catheter through the defect and the finding of a step-up in oxygen content of blood obtained from the right atrium, represents the most specific and conclusive diagnostic tool. Mild to moderate pulmonary hypertension was present in all but one patient. This is in contrast to the usual finding of normal pulmonary artery pressure in the young age group. Nevertheless, we found no relationship between age and severity of pulmonary hypertension. In fact, our oldest patient, aged seventy years, had markedly increased pulmonary blood flow, normal pul-

monary vascular resistance and minimal pulmonary hypertension.

Since it has recently been demonstrated that successful surgical closure of atrial septal defect in the elderly is possible,[5,6] recognition of this disorder in this age group is of more than academic interest. However, the role of associated cardiac or pulmonary disease must be carefully evaluated before surgery is recommended.

One can only conjecture whether arteriosclerotic or other cardiac disturbances may play a role in the genesis of the less common arrhythmias and conduction disturbances in these older patients. Also unanswered is the question whether earlier recognition and repair of the atrial defect may prevent the subsequent onset of symptoms and signs.

Summary and Conclusions

1. Ten cases of proved atrial septal defect masquerading as other forms of cardiopulmonary disease in middle-aged and elderly patients are presented. With increasing age, superimposed hypertensive or arteriosclerotic heart disease or pulmonary disease may mask an associated congenital atrial septal defect and may be the mechanism which initiates symptoms.

2. The occurrence of atypical physical findings, transient or persistent arrhythmias, and various conduction disturbances is stressed. The diagnosis should be suspected in patients with such atypical findings, who also have accentuation and splitting of the second pulmonary sound, and radiologic prominence of the pulmonary vasculature and its activity. Cardiac catheterization studies are necessary for definitive diagnosis.

3. Our hemodynamic data support previous observations that large pulmonary blood flow over many years does not necessarily lead to severe pulmonary hypertension. Surgical closure is, therefore, feasible in this age group. The significance of associated cardiac and pulmonary disease, however, must be considered.

Acknowledgments

We wish to express our appreciation to Drs. M. S. Belle, J. J. Hutson and W. L. Wagener, for permission to include their patients in this study; to Dr. R. S. Litwak, for the findings in the two patients who underwent cardiac surgery; to Dr. P. R. Rezek, under whose direction the postmortem findings in one patient were made available; and finally to Dr. R. J. Boucek for his helpful and critical review of the original manuscript.

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Experimental Study

Sympathogenic Origin and Antiadrenergic Prevention of Stress-Induced Myocardial Lesions*

WILHELM RAAB, M.D., F.A.C.C., ERNEST STARK, M.D., WILLIAM H. MACMILLAN, PH.D. *and* WILDA R. GIGEE, A.B.

Burlington, Vermont

ONLY A FEW years ago, the presence of necrotic and fibrotic foci in the myocardium was attributed most often to mechanical interferences in coronary flow from coronary sclerotic changes, hypotension-induced coronary ischemia or mythical coronary "spasms." Of course, a major reduction of coronary flow is an important and often decisive cause of myocardial degeneration, but biochemical neurohormonal influences on myocardial metabolism can, likewise, cause severe myocardial lesions, even without any impairment of the coronary circulation. This fact, known since 1907 when Josué[1] described epinephrine-induced necroses of the heart muscle, remained excluded from clinical thinking until the traditional mechanistic viewpoint was finally abandoned, at least by some, under the impact of experimental, clinical and anatomic observations which clearly demonstrated chemically-induced necrotic and fibrotic changes in hearts with normal coronary vessels.

A large body of evidence was contributed by Selye.[2] By combining the administration of certain corticoids, especially 2-alpha-methyl-9-alpha fluorohydrocortisone (fluorocortisol), with various types of stress, he regularly produced severe disseminated necroses in the ventricles of the rat heart. He expressed puzzlement at the incongruousness of stresses, such as prolonged restraint, caloric, surgical and bacteriotoxic stress, vagotomy and injection of epinephrine and norepinephrine, all of which elicited the same type of cardiac necroses in corticoid-preconditioned hearts. In Selye's belief, these stresses have nothing identifiable in common and are, therefore, described by him as "unspecific."

As far as the "first mediator"[3] in the stress syndrome is concerned, namely the mechanism by which stressful derangements in a multitude of tissues put the corresponding hypothalamic, neurovegetative and endocrine responses into effect, three principal points ought to be kept in mind:

1. The multiplicity of areas and tissues from which hypothalamic stress responses are elicited justifies the assumption that afferent nervous pathways, ultimately converging in the hypothalamus (rather than any blood-borne humoral agents), convey the first stress signal to the neurovegetative and endocrine systems.

2. Reflex hypothalamic stimulation elicits discharges of adrenergic catecholamines from the adrenal medulla and from the peripheral sympathetic nerve terminals.[4,13] They are manifested by an augmentation of plasma catecholamine levels.[5–12]

3. The increased amount of discharged circulating cathecholamines, although a regular and characteristic feature of the early "neurogenic" phase of the stress syndrome,[5,14–27] is not

* From the Division of Experimental Medicine and the Departments of Pathology and Pharmacology of the University of Vermont, Burlington, Vermont. This study was aided by research grants from the U. S. Public Health Service (H-2169 from the National Heart Institute and B-2673 from the National Institute for Neurological Diseases and Blindness).

the decisive factor in the activation of the pituitary-adrenocortical axis (liberation of ACTH and corticoids)[8,28–33] but is responsible for the accompanying adrenergic cardiovascular reactions (augmented heart rate and blood pressure, electrocardiographic changes).

Although the pathogenic implications of the stress-induced adrenergic cardiac features have been almost disregarded in the existing literature on stress, they are of importance for the understanding of stress-induced injury to the myocardium.[2,34–37] Augmented catecholamine discharges into the circulation have been directly observed under such diverse stresses as tumbling trauma,[18] pain,[6] restraint,[6] exposure to cold and heat,[6,34] exercise,[6,16,19,26,38] emotional stress,[21,39] increased intracranial pressure,[15,20] hemorrhage,[6,22] hypercapnia,[25,27] infections and bacteriotoxic effects,[6,24] insulin overdosage,[6,23,26] peptone shock,[6] histamine[6,17] and asphyxia.[6]

It has long been known that adrenergic catecholamines are tissue-necrotizing agents, and that their administration produces structural lesions of the myocardium.[14,40–47] While large doses of epinephrine, norepinephrine and isoproterenol were required to produce these experimental lesions, a marked potentiation of their cardiotoxic effects was observed[2,48–50] after pretreatment with mineralocorticoids, especially with fluorocortisol. The development of stress-induced myocardial necrotic lesions was likewise greatly accentuated by combination with mineralocorticoid administration.[2] Vagotomy, which automatically causes a marked adrenergic preponderance in cardiac function and metabolism,[51] also elicited myocardial necroses,[2] whereas transsection of the cervical cord which interrupts the stress reflex arc, prevented them.[2]

To consolidate our concept that stress-induced catecholamine interference in cardiac metabolism represents the common denominator in the stress-induced necrotizing cardiopathies under various conditions, we decided to investigate the influence of antiadrenergic drugs on the degree of stress-induced myocardial lesions in rats which had been conditioned by pretreatment with fluorocortisol or dihydrotachysterol or thyroxine. According to Selye,[2] the corticoids sensitize the heart by directly affecting myocardial metabolism, whereas dihydrotachysterol tends to promote both coronary vascular obstructions and myocardial calcifications in conjunction with adrenal corticoids,[52,53] in apparent analogy to similar effects of the parathyroid hormone.[54] Thyroxine potentiates the functional and metabolic influences of the catecholamines *per se* on the heart muscle.[55,56] In one group of rats, we replaced the physiologic stress types that were used in most of our experiments by the administration of nicotine, which also mobilizes catecholamines.[6,23,57]

Antiadrenergic agents used were the following: (1) reserpine (Serpasil®) which depletes catecholamines in the heart and other tissues,[58–61] and protects partially against the fatal effects of tumbling trauma[59] and pulmonary edema from high oxygen pressure;[83] (2) guanethidine (Ismelin®) which depletes myocardial catecholamines;[62–64] (3) mecamylamine (Inversine®), a ganglionic blocker which reduces catecholamine discharges;[65] (4) chlorpromazine (Thorazine®) which is believed to suppress subcortical reflex stimulations of the sympathoadrenergic system[66–68] and which protects against death from tourniquet trauma, heat,[69] bacteriotoxins,[70] and pulmonary edema;[83] and (5) Dibenamine® which chiefly blocks the action of circulating catecholamines[71,72] and like other adrenergic blocking agents,[70,73] protects against tumbling and other stresses.

Norepinephrine assays on the hearts of a number of our experimental animals were carried out under analogous experimental conditions, even though the degree and speed of the liberation and turn-over of catecholamines in the heart muscle can be reflected only to a limited extent in their concentration at the moment of the animal's death.[74] The heart muscle (in contrast to the striated muscles) possesses a remarkable ability to absorb and accumulate enormous quantities of catecholamines, if they are injected in large doses.[75] The absorption of smaller amounts may remain undetectable by conventional methods,[76,77] but it could be ascertained by using labeled catecholamines.[78] Myocardial norepinephrine has been found to be augmented after electrical stimulation of the cardiac sympathetic nerves,[75,79] myocardial epinephrine after exercise,[80] and total myocardial catecholamines were increased after cold exposure, exercise,[14] insulin overdosage[14,80] and trauma.[81]

Material and Methods

Female Sprague-Dawley rats, weighing approximately 100 gm. and fed on Purina Fox Chow, were used. In close adherence to Selye's technic,[2] stress was produced in most instances by restraining the rats on a board for fifteen hours. In a smaller group, cold stress was applied by immersing the rats in ice water twice for three minutes each, at an interval

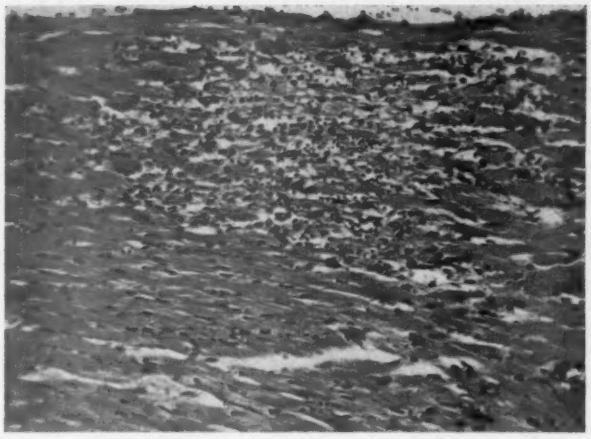

FIG. 1. Myocardium displays severe reaction to stress in fluorohydrocortisone-pretreated rat. Focal areas of necrosis and intense cellular inflammatory reaction. (Classified as grade 3.) Low power (approximate original magnification ×100).

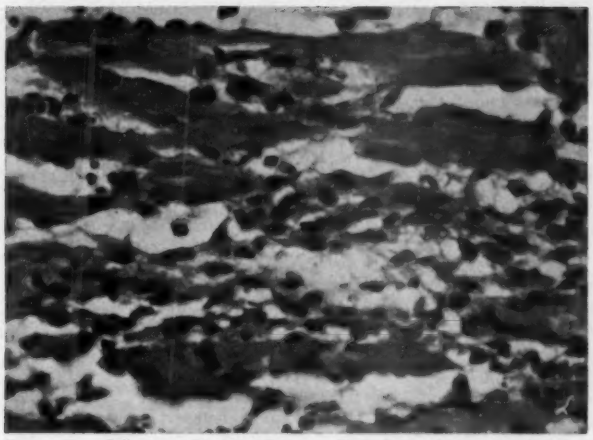

FIG. 2. Myocardium shows fragmentation and disappearance of many muscle cells. The cellular reaction is lymphocytic, monocytic and fibroblastic. Sarcolemmal proliferation is probably present but this is difficult to distinguish from fibroblastic proliferation. High power (approximate original magnification ×400).

of seventeen hours. In an additional group of animals, nicotine bitartrate in oil was administered intramuscularly in two doses of 0.1 mg. each at an interval of seven hours.

Hormone pretreatments before stress included: (1) 2-alpha-methyl-9-alpha-fluorohydrocortisone (fluorocortisol), 500 μg., subcutaneously injected in 0.2 ml. of water on each of seven successive days; (2) dihydrotachysterol (Calciferol), given by stomach tube on three successive days (150 mg. twice on the first two days, 150 mg. once on the third day); (3) thyroxine (Synthroid®), administered by stomach tube in daily doses of 0.3 mg. each, on eight successive days.

Antiadrenergic medication consisted of (1) reserpine, 0.4 μg., injected subcutaneously daily on seven or fourteen successive days; (2) mecamylamine hydrochloride, 1.25 mg., administered by stomach tube twice at intervals of six and twenty-four hours in conjunction with restraint or cold stress; (3) chlorpromazine, 0.2 mg., injected intramuscularly twice on the same day at an interval of ten hours; (4) Dibenamine, 5 mg., injected subcutaneously twice on the same day at an interval of six hours; (5) guanethidine, 1 mg., injected subcutaneously daily on seven consecutive days.

The time relations were arranged so that the stresses were applied on the last days of the hormonal pretreatment. Reserpine treatment coincided with the hormone administration periods; in some instances it preceded them, in addition, by one week. Mecamylamine was given six hours and immediately before restraint, and on two evenings preceding the day of cold stress.

Anatomic Studies: For morphologic examination of the hearts, the animals were sacrificed by decapitation six hours after termination of restraint, twenty-four hours after termination of cold stress, and twenty hours after the second dose of nicotine. For norepinephrine assay, they were sacrificed in most instances immediately after termination of restraint, in some others, six hours later.

Histologic examinations as well as norepinephrine determinations in the heart muscle were carried out "blindly;" i.e., without knowledge of the preceding experimental conditions.

The structural heart lesions were judged exclusively on their microscopic appearance. At least two different sections of each heart were prepared, taking the longitudinal half section from base to apex through the septum. The severity and extent of the lesions were graded from 0 to 3. Severity was estimated primarily by the cellular reaction and, to a lesser extent, by the appearance of the muscle fibers. The former varied from neutrophilic in the more acute reactions to mononuclear cellular accumulation and often histiocytic proliferation with occasional participation of sarcolemma cells. If the focal areas of these changes were few and small, a lower grade of lesion was assigned, whereas a more extensive involvement was classified as a higher grade.

While the appearance of damaged muscle cells with loss of striation and staining quality was fairly clearcut, we found it not advisable to rely on this feature alone in the absence of distinct inflammatory reaction, since, occasionally, artefacts may also resemble necrotic or damaged muscle cells.

The pressor active principle of tissue extracts was determined by biological assay using the pithed rat blood pressure method.[82] Male rats, Wistar strain, weighing 190 to 220 gm., were given atropine sulfate (1 mg. per 100 gm.). Ten minutes later the animals were deeply anesthetized with ether. A tracheal cannula was inserted and the animal pithed by passing a steel rod through the eye socket and down the spinal canal. Artificial respiration was given at a rate of 90 per minute. A polyethylene cannula (PE-60) was inserted into the left external jugular

TABLE I
Morphologic Lesions

Group	Types of Experiments	No. of Rats	Morphologic Lesions					
			Average Grade per Group	Grade 3 (per cent per group)	Grade 0 (per cent per group)	Standard Deviation	p	Groups of Reference
A	No treatment	17	0.0	0	100	±0.00	...	..
B	Restraint	10	0.0	0	100	±0.00	...	..
C	Fluorocortisol	10	0.0	0	100	±0.00	...	..
D	Fluorocortisol + restraint	27	2.4	63	7	±1.13	<0.01	C
E	Fluorocortisol + restraint + reserpine (1 week)	16	1.0	6	25	±0.08	<0.01	D
F	Fluorocortisol + restraint + reserpine (2 weeks)	8	0.8	0	25	±0.80	<0.01	D
G	Fluorocortisol + restraint + mecamylamine	19	0.6	0	47	±0.79	<0.01	D
H	Fluorocortisol + restraint + reserpine (1 week) + mecamylamine	15	0.5	0	53	±0.61	<0.01	D
I	Fluorocortisol + restraint + chlorpromazine	18	1.4	17	17	±1.07	<0.01	D
J	Fluorocortisol + restraint + dibenamine	8	1.5	25	13	±1.03	0.017	D
K	Fluorocortisol + restraint + guanethidine	9	1.1	22	33	±1.24	<0.01	D
L	Fluorocortisol + cold stress	10	1.3	10	30	±1.13	<0.01	C
M	Fluorocortisol + cold stress + mecamylamine	8	0.4	0	62	±0.73	0.08	L
N	Fluorocortisol + nicotine	10	0.8	0	20	±0.42	<0.01	C
O	DHT + cold stress	9	0.9	22	56	±1.27	0.02	A
P	DHT + cold stress + mecamylamine	12	0.2	0	83	±0.59	0.16	O
Q	Thyroxine	5	0.1	0	80	±0.30	>0.50	A
R	Thyroxine + restraint	12	0.5	0	58	±0.78	0.30	Q
S	Thyroxine + restraint + reserpine (1 week)	11	0.2	0	73	±0.41	0.30	R

vein for intravenous injection of the test solutions. The right common carotid artery was cannulated and connected to a mercury manometer for recording blood pressures. The pressor active principles were compared with standard concentrations of norepinephrine, and are expressed as μg. norepinephrine per gm. of tissue. No differential assay for epinephrine was performed.

RESULTS

Myocardial Lesions: As shown in Table I, we could confirm Selye's[2] observations that neither fluorocortisol treatment alone nor stress alone produces any demonstrable structural lesions of the myocardium, whereas widespread cardiac necroses occurred in most of the fluorocortisol-pretreated rats exposed to the stress of restraint (Figs. 1, 2). Cold stress and nicotine were considerably less effective than restraint under analogous pretreatment.

The tendency toward restraint-induced myocardial changes in fluorocortisol-pretreated rats was moderately to markedly diminished by drugs with antiadrenergic properties in the following order of increasing effectiveness: Dibenamine (lesions reduced 38 per cent); chlorpromazine (reduced 42 per cent); guanethidine (reduced 54 per cent); reserpine (one week: reduced 58 per cent; two weeks: reduced 67 per cent); mecamylamine (reduced 75 per cent); reserpine plus mecamylamine (reduced 79 per cent) (Fig. 3). The myocardial lesions produced by cold stress in rats pretreated

TABLE II
Norepinephrine Content of the Heart Muscle

Group	Types of Experiments	No. of Rats	Norepinephrine (μg./gm. of tissue)				
			Average per Group	Standard Deviation	p	Groups of Reference	Per Cent Deviations from Normal
A	No treatment	24	0.254	±0.075	...	..	...
B	Fluorocortisol	11	0.258	±0.109	0.50	A	+2
C	Norepinephrine injection	12	0.340	±0.089	0.45	A	+34
D	Restraint	13	0.316	±0.127	0.50	A	+24
E	Fluorocortisol + norepinephrine	11	0.195	±0.510	0.21	C	−23
F	Fluorocortisol + restraint (killed immediately)	10	0.156	±0.053	0.25	D	−39
G	Fluorocortisol + restraint (killed after 6 hours)	8	0.151	±0.031	0.25	D	−41
H	Reserpine	14	0.196	±0.046	0.50	A	−23
I	Fluorocortisol + restraint + reserpine (killed immediately)	10	0.224	±0.071	0.50	F	−12
J	Fluorocortisol + restraint + reserpine (killed after 6 hours)	10	0.193	±0.400	0.50	G	−24
K	Fluorocortisol + restraint + guanethidine	10	0.140	±0.048	0.50	F	−45
L	Fluorocortisol + restraint + chlorpromazine	10	0.275	±0.128	0.50	F	+8
M	Fluorocortisol + restraint + mecamylamine	10	0.261	±0.086	0.45	F	+3

by fluorocortisol and dihydrotachysterol (DHT) were likewise diminished by mecamylamine (69 per cent and 77 per cent, respectively). The relatively mild myocardial lesions, elicited by restraint in thyroxine-pretreated rats, also appeared to be reduced by reserpine but these latter data were statistically less significant.

The norepinephrine concentration in the heart muscle (Table II) was not affected by fluorocortisol but was augmented 34 per cent by in-

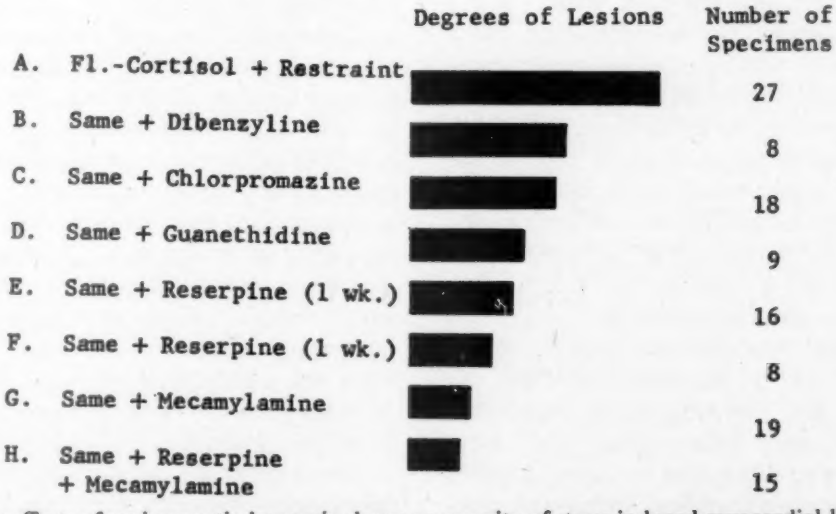

FIG. 3. Average effects of various antiadrenergic drugs on severity of stress-induced myocardial lesions in fluorohydrocortisone-pretreated rats.

jection of norepinephrine, and 24 per cent by restraint. In animals pretreated with fluorocortisol on the contrary, injection of norepinephrine and restraint were followed by a diminution of the myocardial norepinephrine. Reserpine and guanethidine also reduced the cardiac norepinephrine content in restrained animals pretreated with fluorocortisol, whereas chlorpromazine and mecamylamine left it practically unchanged.

Although the statistical significance of the results of various individual experimental subgroups concerning myocardial norepinephrine was only borderline or less, there appeared to be a more significant equidirectional trend in the categories of mutually related experimental procedures, such as the increase of myocardial norepinephrine in conditions long known to produce this effect (injection of norepinephrine,[75,78] and stress[14,75,80]), the diminution of cardiac norepinephrine after administration of catecholamine-depleting drugs (reserpine[58–61] and guanethidine[62–64]), and the norepinephrine loss from the hearts of rats pretreated with fluorocortisol that had been subjected to otherwise norepinephrine-augmenting procedures, namely, the administration or liberation (through stress) of norepinephrine.

Comments

Antiadrenergic agents of various types (catecholamine-depleting, adrenergic blocking, ganglionic blocking, centrally inhibiting) protected the heart muscle of rats, preconditioned with corticoids, DHT or thyroid hormone, with different degrees of effectiveness against stress-induced necrotizing changes which were otherwise elicited by restraint and cold stress. Since all stressful situations are accompanied by a reflex discharge of adrenosympathogenic catecholamines, known to possess potentially cardiodestructive properties, the evidence suggests that these catecholamines play a decisive role in the development of myocardial lesions under stress in animals preconditioned by certain hormones.

It seems significant that those antiadrenergic agents whose action is presumably limited to an inhibition of the catecholamine-mobilizing reflex arc at the hypothalamic level (chlorpromazine[66–68]) or to blockade of only the circulating but not the neurogenic intramyocardial catecholamines (Dibenamine[71,72,76]) were the least effective in protecting the heart muscle, whereas those with ganglionic blocking (mecamylamine) or direct myocardial catecholamine-depleting action (reserpine, guanethidine[58–64]) and, especially, a combination of the latter two types of drugs, proved most effective.

Bioassay of norepinephrine in the heart muscle provided some additional clues. It confirmed earlier findings concerning a tendency of the heart muscle to accumulate injected[75,78] and stress-liberated[14] catecholamines. By contrast, a marked diminution of the cardiac norepinephrine content was observed after norepinephrine injection and after stress in animals pretreated with fluorocortisol (fluorocortisol *per se* neither caused myocardial lesions nor altered the myocardial norepinephrine content). Since the combination of fluorocortisol pretreatment with injection of norepinephrine[48] or stress[2] produces severe structural myocardial changes, it appears probable that the losses of cardiac norepinephrine are due to the loss of the normal ability to retain catecholamines in the necrotized areas of the myocardium.

The mechanism of this latter cardiac norepinephrine depletion is quite different from that which occurs under the influence of reserpine and guanethidine.[58–64] When both norepinephrine-depleting procedures, namely, (1) the cardiac necrotizing corticoid-stress exposure and (2) the administration of reserpine or guanethidine, were combined, no clearly additive norepinephrine-depletion was observed, presumably because of the cardiac tissue-protecting effect of reserpine and guanethidine. The stress-induced accumulation of norepinephrine was apparently prevented in part by the drugs and in part by the (mitigated) tissue destruction, both of which are norepinephrine-depleting.

Chlorpromazine and mecamylamine did not exert any directly catecholamine depleting action in the heart itself but, by interfering with neurogenic catecholamine discharges, reduced myocardial injury in corticoid-pretreated animals. They kept the cardiac norepinephrine concentration nearly unchanged.

A general review of our findings strongly supports the concept that the stress-induced structural changes of the heart muscle in animals, pretreated with fluorocortisol, dihydrotachysterol or, possibly, thyroxine, are directly attributable to the stress-induced reflex liberation of adrenosympathogenic catecholamines.

The possibility of clinical analogies to the previously discussed cardiotoxic combinations of stress-induced catecholamine discharges and

sensitizing hormone overactivity, especially concerning adrenal corticoids, and the prospect of clinical heart protection by antiadrenergic drugs, must be seriously considered. Reserpine proved effective in our experiments in doses equivalent to those used in human therapy (they corresponded to approximately 0.28 mg. daily for a man weighing 70 kg.). Recognition of the fundamental involvement of cardiotoxic adrenosympathogenic catecholamine action in the origin of stress-induced myocardial degeneration is likely to open promising new avenues of research in the vast but largely unexplored field of neurogenic and hormonal cardiac pathology.

Summary

Moderate to nearly complete protection of the heart muscle against stress-induced necrotizing myocardial lesions in corticoid- or dihydrotachysterol-preconditioned rats was achieved through administration of drugs with direct or indirect antiadrenergic properties: reserpine, guanethidine (catecholamine depletion); mecamylamine (ganglionic blockade); chlorpromazine (inhibition of sympathetic-stimulating reflexes at the hypothalamic level), and Dibenamine (blockade of circulating catecholamines).

In otherwise untreated animals, the norepinephrine content of the heart muscle was increased by injection of norepinephrine as well as by its liberation under stress. In corticoid-pretreated rats, by contrast, both norepinephrine injection and stress were followed by losses of norepinephrine from the heart, presumably due to the extensive destruction of myocardial tissue under these conditions. Antiadrenergic drugs produced intermediary effects upon the cardiac content of norepinephrine by counteracting its accumulation as well as its depletion resulting from tissue necrosis.

It is concluded that the stress-induced severe myocardial structural lesions in hormone-preconditioned animals are directly attributable to the reflex liberation of potentially cardiotoxic adrenosympathogenic catecholamines which accompanies all stressful situations.

Acknowledgment

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New Method

Continuous Electrocardiograms

Electrodes and Lead Systems*

JOHN S. GILSON, M.D., AND RICHARD B. GRIFFING, M.D.,
WITH THE TECHNICAL ASSISTANCE OF WYOMA HOOPS

Great Falls, Montana

ANALYSIS OF continuous pulse and electrocardiographic patterns is now practical, using tape recording devices and rapid playback technics developed at the Holter Foundation's laboratory in Helena, Montana.[1] Two preliminary associated problems involved in utilizing these technics are discussed in this paper: (1) developing a method of attaching electrodes to the skin so that they will be tolerable for periods up to eighteen hours or more and will also be able to function during ordinary daily activity; and (2) testing a lead system which will produce patterns similar to those of conventional chest leads yet be suitable for use during ordinary activity. A recent paper by Freiman et al.[2] discusses records taken during activity and describes both new electrodes and a new system of electrode placement. The same group reported recently on studies using that technic.[3]

ELECTRODES AND ELECTRODE ATTACHMENT

The tape recording devices devised at the Holter Laboratory work best at resistances below 20,000 ohms, whereas conventional direct writing electrocardiographic machines will work satisfactorily at resistances up to and beyond 50,000 ohms. Electrodes in contact with both the skin and electrode paste for a period of many hours have not previously been studied to our knowledge. Although we considered the use of needle electrodes inserted subcutaneously we arbitrarily ruled out this technic until we had thoroughly explored the use of surface contact. The lead-Rezifilm-gauze electrode described in this paper is believed to be satisfactory in all respects for periods up to twenty-four to forty-eight hours at least.

Electrodes tested and discarded during our studies are illustrated in Figure 1. The bulk of the electrodes, along with our inability to devise methods for holding them in place, caused us to discard the conventional, flat, German-silver electrode, the Welsh suction electrode,* and the Plastrode.† Wandering of the base line with movement caused us to abandon the Rowley electrode[4] and the sponge electrode because such wandering is incompatible with our playback devices necessary for rapid analysis of records covering many hours. Very high resistances caused us to cease observations on the silver collodion electrode.‡ Skin intolerance occurred often enough with an ordinary dime as the electrode that we stopped using this readily-available source of molded silver. Although separate studies of the properties of sheet aluminum, pure silver and metallic lead sheets did not reveal irritation of the skin with any of these materials, the most consistently low resistances, which remained low over a period of twenty-four to thirty-six hours, were observed with metallic lead. Because metallic lead is inexpensive, malleable, nonirritating and sustains a prolonged low resistance in contact with the skin and electrode paste, we have used lead in our recommended electrode.

Our lead-Rezifilm-gauze electrode (Fig. 2) satisfies the need for a flat, comfortable, electrically

* Sanborn Company, Waltham, Massachusetts.
† Bowen & Company, Inc., Bethesda, Maryland
‡ Gulton Industries, Inc., Metuchen, New Jersey.

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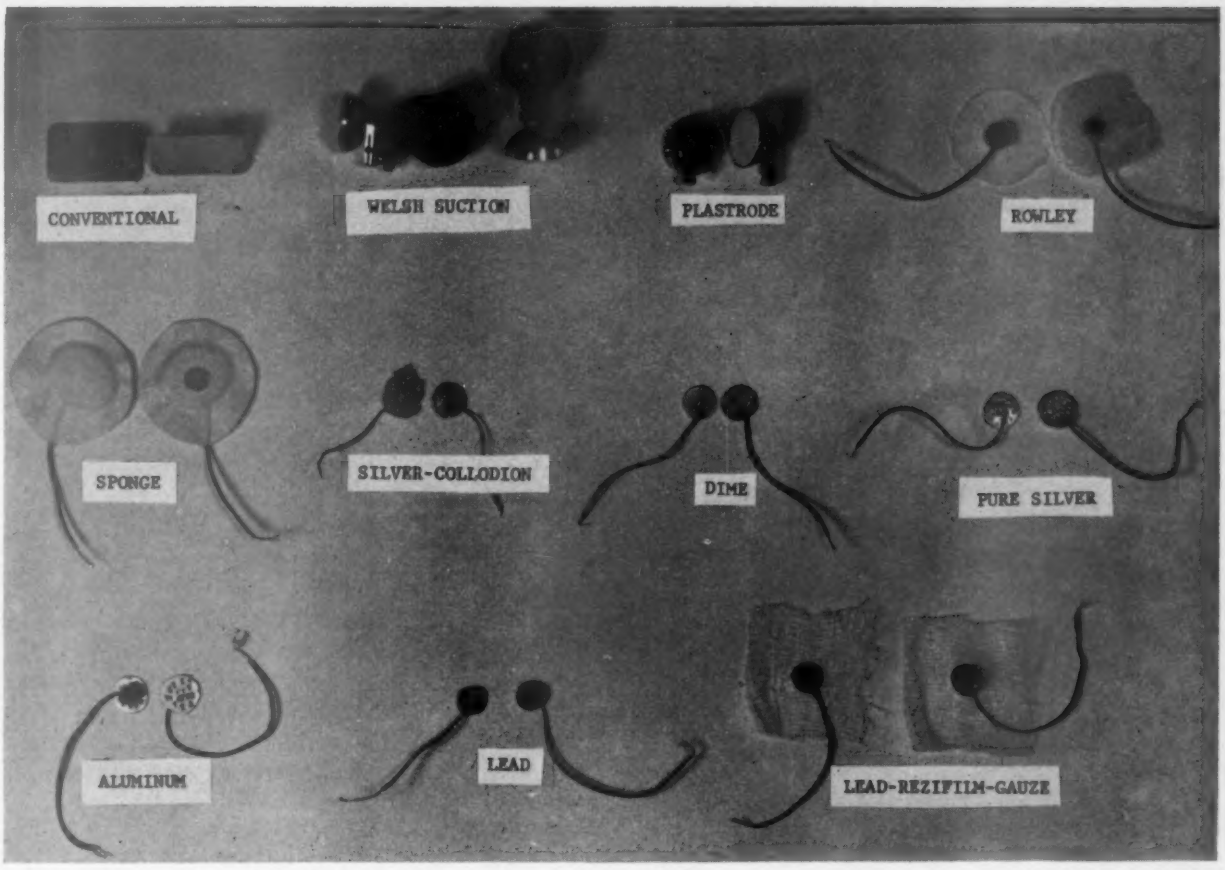

FIG. 1. Electrodes studied. Each is shown as a pair, the left showing as it would appear on the skin, the right as it looks turned upside down. The conventional, Welsh suction, and Plastrode are commercially available and in common use. Rowley electrode is a section of tubing cupped at one end and open at the other, filled with electrode paste, into which the wires are run. The open end of the tube is cemented to gauze and the gauze cemented to skin in order to make contact. Sponge electrode contains a sponge of plastic foam saturated with electrode paste into which a wire is run. The sponge is contained in an adhesive envelope open to the skin. It is held in place with tape and elastic bandages. Silver collodion is a wire mesh electrode pressed in place with a silver collodion paste. The dime, sheet silver, sheet aluminum and sheet lead are simply discs of these metals indented slightly to provide tiny reservoirs for electrode paste. Lead-Rezifilm-gauze is described in the text.

satisfactory electrode. Through the note by Browne[5] we learned of Nobecutane which is marketed in this country as Rezifilm.* This is a "spray bandage" material of great strength which has not produced any skin irritation in our subjects so far. A base of the material is sprayed on the skin after protecting the previously abraded electrode area with adhesive tape. After removing the tape and allowing the Rezifilm to become "tacky," the slightly cupped, metallic lead electrode, which has a square of surgical gauze rubber-cemented to its outside, is laid in place over a dab of electrode jelly, patting the gauze into the tacky Rezifilm snugly. The area is then resprayed and allowed to dry. By this means the electrode is firmly attached to the skin. After a few moments it

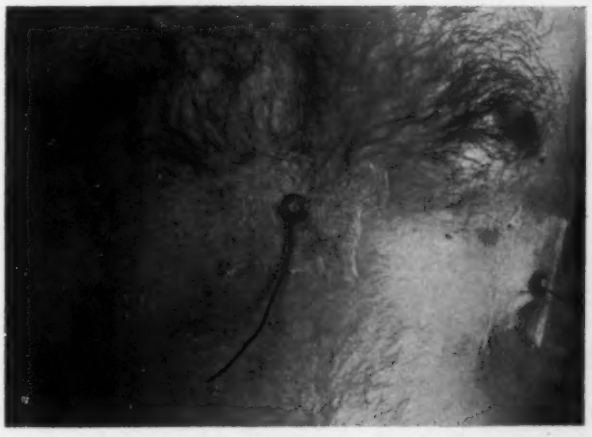

FIG. 2. The lead-Rezifilm-gauze electrode as it looks on the subject. Although it looks loose, it is still in intimate contact with the skin on the far left of the subject despite a strong tug on the wire leading from it. The gauze is embedded in the Rezifilm spray film but the film does not show.

* E. R. Squibb & Sons, New York, New York.

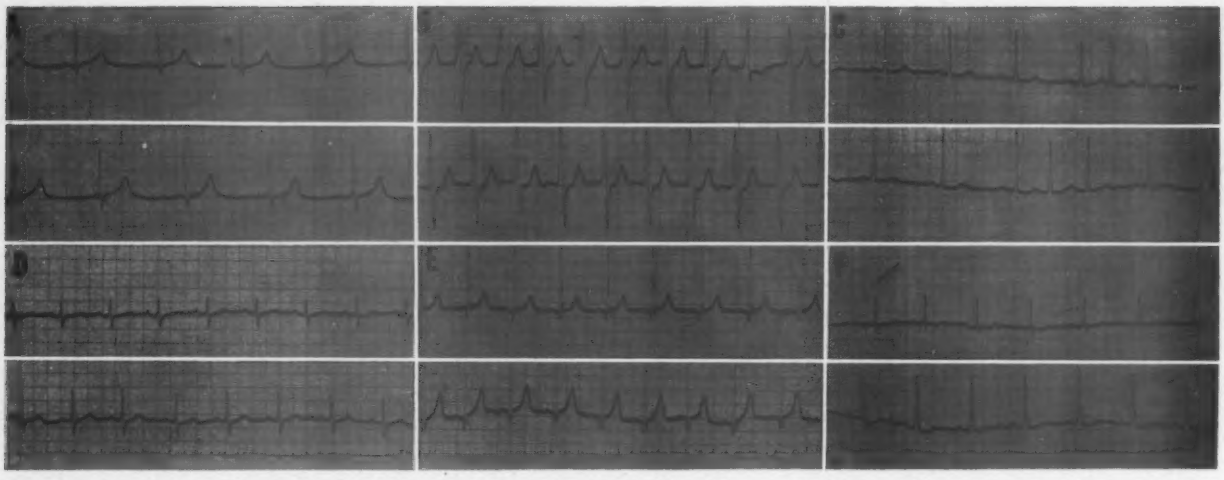

FIG. 3. Comparison of standard V_5 (upper tracing in each pair) with our C_5R-C_5 lead (lower tracing in each pair). Pairs A, B and C (top two rows) show the qualitatively similar tracings usually seen. Pairs D, E and F (bottom two rows) show instances of qualitatively dissimilar tracings. Pair A = ten year old boy; similar patterns in both positions. Pair B = fifty-five year old man; similar patterns in both positions. Pair C = eighty year old woman; similar patterns in both positions. Pair D = seventy-seven year old man; taller R, smaller S and taller T in our C_5R-C_5 lead than in standard V_5. Pair E = sixty-four year old woman; taller T waves in our C_5R-C_5 lead. Pair F = ten year old boy; taller R wave and absent S wave in our C_5R-C_5.

causes somewhat less discomfort than ordinary adhesive tape would cause if covering the same area. The contact area remains moist and of low resistance for up to thirty-six hours, and tolerates ordinary activities of all types including bathing without loss of effectiveness.

The electrode is relatively easy to apply and with practice the application of three electrodes takes approximately seven minutes for an experienced technician. Removal of the electrodes is readily performed without discomfort by using a pad of acetone to dampen the area of Rezifilm.

Resistances have ranged from 2,000 to 14,000 ohms in 230 tests on twenty-nine subjects who had the electrodes on for periods of five to thirty-six hours.

During exertion and motion there is a minimum of motion of the electrode against the skin. The electrode tends to move with the skin because of the wide area of attachment of the gauze which is in turn closely attached to the electrode as noted in Figure 2. Considerable pull can be applied to the lead wire without separation of the electrode from intimate contact with the skin (Fig. 2, far right electrode). During the course of exertion the base line remains relatively constant, apparently because of close, unchanging contact. A stable base line is a significant advantage, both in observing exercise electrocardiograms and in utilizing the analysis and playback devices developed at the Holter Laboratory.

ELECTRODE POSITIONS

The reports of Freiman and Abarquez et al.[2,3] emphasize the need for electrode positions which will minimize muscle potential by placing electrodes over bony prominences. In addition we have preferred a symmetrical lead system to further reduce muscle potential and have utilized the trunk rather than the arms because of the lack of asymmetric motion in the trunk in ordinary activity.

The lead chosen by us we have termed "symmetric C_5R-C_5" to indicate the electrode positions. This lead puts one electrode at any of the usual precordial sites on the left side of the chest, such as positions 4, 5 or 6 (we use position 5). The other electrode is put similarly and symmetrically at the same position on the right side of the chest. In using this system a ground wire was connected to an electrode fastened to the chest over the ensiform (Fig. 2). In this system the two lateral positions are connected to the electrocardiograph through any convenient lead (such as right electrode to right arm wire, left electrode to left arm wire, with recording through lead I setting of the machine).

Comparison of C_5R-C_5 Lead and V_5: To compare this lead with standard V_5 we performed studies leaving our C_5 electrode in place, changing the connections so that the machine now recorded V_5 on the left side of the chest. We obtained first a tracing from "C_5R-C_5 lead" and then after reconnecting the machine we obtained V_5 from the same precordial position.

In fifty patients the patterns obtained by our symmetrical electrode C_5R-C_5 were qualitatively *identical* to V_5 in about 40 per cent. The magnitude of the R wave in our symmetrical C_5R-C_5 *exceeded* that in conventional V_5 in sixteen out of fifty subjects and ranged as high as twice the amplitude seen in V_5. The magnitude of the R wave was less than that seen in V_5 in seventeen subjects but never went below two-thirds of the amplitude of the R wave in V_5 (Fig. 3). Comparison of T wave magnitudes were of similar degree. The S-T segment was positioned identically in the two lead systems with never more than 1 mm. difference in take-off level.

Comparison With Method of Freiman et al.: In order to compare our results on lead systems with those of Freiman et al.[2] we have duplicated their observations on seventeen subjects of our own (using our lead-Rezifilm-gauze method of attaching electrodes and applying them according to their "A" and "B" system) with essentially similar findings so far as electrocardiographic patterns are concerned. We also tried an additional lead (which we called "C") with electrodes placed over the second thoracic vertebra and over the V_5 position on the left side of the chest. This lead system gave findings similar to their lead A in these seventeen subjects.

Summary and Conclusions

1. In the search for an electrode which could be worn over a long period of time, and which would also provide low resistance with a stable base line for the taking of long-term continuous electrocardiograms, some nine different electrodes have been tested. Eight of these have been rejected, either because of their bulk which renders attachment to the skin over long periods of time quite difficult, because of resistances beyond the range tolerated by our recording and playback equipment, or because of a wandering base line produced during movement.

2. An electrode utilizing lead as the metallic contact, plus ordinary electrode paste, and held in place with gauze impregnated with a spray film has proved to be satisfactory for continuous recording of electrocardiograms over a period of many hours with subjects involved in ordinary activities.

3. A symmetrical lead system is demonstrated which gives an electrocardiographic pattern qualitatively similar to that usually obtained with the unipolar chest leads. The differences from usual chest leads are quantitative but are not great enough to require an entirely new approach to those patterns.

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Review

The Pathologic Anatomy of Mixed Levocardia

A Review of Thirteen Cases of Atrial or Ventricular Inversion With or Without Corrected Transposition*

MAURICE LEV, M.D., F.A.C.C. *and* URSULA F. ROWLATT, D.M. (OXON.)

Chicago, Illinois

MIXED LEVOCARDIA is that condition in which the base-apex axis points toward the left and downward (as normally) but the atria and ventricles do not correspond.[1] We have recently studied thirteen such cases which form the basis of this report.

HISTORICAL REVIEW

There are two types of mixed levocardia discussed in the literature: (1) that with ventricular inversion and (2) that with atrial inversion. Many cases of ventricular inversion are also discussed under the term "corrected" transposition. Most cases of atrial inversion are included under the term levocardia or isolated levocardia. The details of the cases of ventricular inversion[1-29] reviewed by us are presented in Table 1. Only those cases in which identification of chambers could reasonably be inferred are reviewed. Cases with an absence of the ventricular septum are thus excluded, since absolute diagnosis of the chambers depends on the topography of the septum.[1] Reported cases with atrial inversion are all included under one type of isolated levocardia, which has been reviewed elsewhere.[30,31]

From Table 1 it can be seen that there are two types of mixed levocardia with ventricular inversion described in the literature: (1) that with complete (noninverted) transposition (cases of Walshe[2] and Stoltz[3]) and (2) that with inverted transposition (all other cases). The term transposition, as previously used by Abbott,[32,33] Spitzer,[34,35] Lev and Saphir,[36,37] Lev,[38,39,40] and Harris and Farber,[17] implies any abnormality in the relative positions of the aorta and the pulmonary artery with respect to each other and with respect to the chambers from which they arise. As so defined, this term is applicable to hearts in pure levocardia; that is, hearts with normal axis and normal relationship of chambers. As so defined, this term cannot apply to mixed levocardia and dextrocardia. When used in mixed levocardia the term transposition implies only an abnormality in the relative positions of the aorta and pulmonary artery. The term inverted transposition is used here in the sense of Spitzer[34,35]: the position of the arterial trunks as seen in the transposition as just defined is, in general, in mirror image to one of the ordinary types of transposition, although altered by hemodynamic circumstance. The term corrected transposition is used here in the sense of Cardell[23]—physiologic correction; that is, the re-establishment of the normal general course of the circulation despite abnormalities in position of chambers or arterial or venous trunks. This term, as used here, does not deny the presence of shunts or defects within this generally normal course of the arterial or venous blood. We agree with Spitzer[35] that the term corrected transposition should be abolished, since semantically it can truly apply only to the

* From the Congenital Heart Disease Research and Training Center, Hektoen Institute for Medical Research, and the Departments of Pathology of the Children's Memorial Hospital, Northwestern University Medical School, University of Illinois Medical School and The University of Chicago School of Medicine. This investigation was supported by a research grant (H-3351) from the National Heart Institute, of the National Institutes of Health, U. S. Public Health Service, Bethesda, Maryland.

TABLE I

Mixed Levocardia with Ventricular Inversion

Author and Year	Sex, Age	Atrioventricular Valves	Origin of Main Coronary Arteries	Relative Position of Efferent Vessels	Pathologic Complexes Associated	Other Cardiac Anomalies
1. Walshe,[3] 1844	M, 10 mos.	Follow the distal chamber	From usual sinuses	Aorta anterior and to the right	Complete transpostion of great vessels	Patent ductus arteriosus Patent foramen ovale
2. Stoltz,[3] 1851	M, 5 days	Follow the distal chamber	...	Aorta anterior and to the right	Complete transposition of great vessels	Patent ductus arteriosus
3. Stoltz,[3] 1851	F, 36 days	Follow the distal chamber	...	Aorta anterior and to the right	Complete transposition of great vessels	Patent ductus arteriosus
4. Rokitansky,[4] 1875	M, 11 mos.	Follow the distal chamber	...	Aorta anterior and to the left	None	...
5. Rokitansky,[4] 1875	F, 4 mos.	Follow the distal chamber	...	Aorta anterior and to the left	None	Patent foramen ovale
6. Tönnies,[5] 1884	...	Follow the distal chamber	Right sinus—right coronary artery. Left posterior sinus—left coronary artery	Aorta anterior and to the left	Ventricular septal defect	Abnormal pulmonary valve. Atrial septal defect
7. Mann,[6] 1889	F, 22 yrs.	Follow the distal chamber	Not stated; right coronary artery forms anterior descending coronary artery	Aorta anterior and to the left	Immense ventricular septal defect forming common ventricle	...
8. Théremin,[7] 1895	M, 4 1/2 mos.	Follow the distal chamber	Right posterior sinus—right artery. Left posterior sinus—left artery	Aorta anterior and to the left	Common ventricle, ventricular septal defect	Patent foramen ovale
9. Lochte,[8] 1898	..., 4–5 yrs.	Follow the distal chamber	Single coronary ostium	Aorta anterior and to the left	Two ventricular septal defects with pulmonary stenosis	Patent foramen ovale Right aortic arch
10. Lochte,[8] 1898	..., 3 yrs.	Follow the distal chamber	...	Aorta anterior and to the left	Ventricular septal defect	...
11. Peters,[9] 1901	F, 25 yrs.	Follow the distal chamber	Right anterior sinus—right coronary artery. Left sinus—left coronary artery	Aorta anterior and to the right	Ventricular septal defect	Patent foramen ovale
12. Geipel,[10] 1903	F, 25 yrs.	Follow the distal chamber	Right anterior sinus—right coronary artery. Left anterior sinus—left coronary artery	Aorta anterior and to the right	Ventricular septal defect	Probe patent foramen ovale
13. Young & Robinson,[11] 1907	F, 2 1/2 yrs.	Follow the distal chamber	...	Aorta anterior and to the left	Complete transposition with pulmonary atresia	Left superior vena cava Atrial septal defect
14. Sato,[12] 1914	...	Follow the distal chamber	...	Aorta anterior and to the left	None	...

Continued next page

TABLE I *Continued*

Author and Year	Sex, Age	Atrioventricular Valves	Origin of Main Coronary Arteries	Relative Position of Efferent Vessels	Pathologic Complexes Associated	Other Cardiac Anomalies
15. Wurm,[13] 1927	M, 3 mos.	Follow the distal chamber	Right anterior sinus—right coronary artery. Posterior—left coronary artery	Aorta anterior and to the left	Fetal coarctation with ventricular septal defect. Left A-V valve apparently insufficient	Patent foramen ovale. Patent ductus arteriosus. Rete Chiari. Fetal coarctation
16. Walmsley,[14] 1930–1	M, 35 yrs.	Follow the distal chamber	Right anterior—right coronary artery. Left anterior—left coronary artery	Aorta anterior and to the left	None	...
17. Stejfa,[15] 1931	M, 19 yrs.	Follow the distal chamber	...	Aorta anterior and to the left	Ventricular septal defect with pulmonary stenosis	Patent foramen ovale. Fine patency of ductus arteriosus
18. Roos,[16] 1936	F, 8½ mos.	Follow the distal chamber	...	Aorta anterior and to the left	Mild coarctation of the aorta	...
19. Harris & Farber,[17] 1939	F, 4½ yrs.	Follow the distal chamber	Right anterior sinus—right coronary. Posterior sinus—left coronary artery	Aorta anterior and to the left	Ventricular septal defect with pulmonary stenosis	Patent foramen ovale
20. Liebow & MacFarland,[18] 1941	M, 9 days	Follow the distal chamber. Neither are typical in configuration	Two coronary ostia arise from the posterior sinus	Aorta anterior and to the left	Ventricular septal defect	Bicuspid aortic valve. Adult coarctation
21. Shaner & Adams,[19] 1951	M, 10 mos.	Both A-V valves irregular in outline	Right anterior—two vessels (right coronary arteries). Left anterior—left coronary artery	Aorta anterior and to the left	Ventricular septal defect with pulmonary stenosis	Persistent ostium primum. Patent ductus arteriosus
22. Lev,[1] 1954	M, 75 yrs.	Follow the distal chamber	Right anterior—both coronary arteries	Aorta anterior and to the left	Hypoplasia of the aorta with fetal coarctation and ventricular septal defect	Patent ductus arteriosus. Patent foramen ovale. Minor anomalies of both A-V valves
23. Edwards,[20] 1954	M, 60 yrs.	Follow the distal chamber	...	Aorta anterior and to the left	Insufficiency of the left A-V valve	...
24. Edwards,[20] 1954	F, 3 yrs.	Follow the distal chamber	...	Aorta anterior and to the left	Insufficiency of the left A-V valve	Patent ductus arteriosus
25. Edwards,[20] 1954	F, 31 yrs.	Regurgitant lesions at base of left A-V valve	...	Aorta anterior and to the left	Insufficiency of the left A-V valve	...
26. Edwards,[20] 1954	F, 2½ mos.	Regurgitant lesions at base of left A-V valve	...	Aorta anterior and to the left	Ebstein's anomaly of left A-V valve. Ventricular septal defect	...

Author and Year	Sex, Age	Atrioventricular Valves	Origin of Main Coronary Arteries	Relative Position of Efferent Vessels	Pathologic Complexes Associated	Other Cardiac Anomalies
27. Platzer,[21] 1955	..., Adult	Follow the distal chamber	Right sinus—right coronary artery. Left posterior sinus—left coronary artery	Aorta anterior and to the left	None	...
28. Becu, Swan, DuShane & Edwards,[22] 1955	F, 3 mos.	Follow the distal chamber	...	Aorta anterior and to the left	Ebstein's anomaly of left A-V valve. Ventricular septal defect	Persistent left superior vena cava draining into the coronary sinus. Patent foramen ovale
29. Cardell,[23] 1956	F, 3 1/2 mos.	Follow the distal chamber	Right anterior sinus—right coronary artery. Posterior sinus—left coronary artery	Aorta anterior and to the left	Ventrical septal defects (3) with pulmonic stenosis	Patent ductus arteriosus. Patent foramen ovale. Bicuspid pulmonic valve
30. Helmholtz, Daugherty & Edwards,[24] 1956	M, 13 yrs.	Follow the distal chamber	...	Aorta anterior and to the left	Ventricular septal defect	Supravalvular ring in relation to left A-V valve. Anomalous insertion of chordae
31. Schaefer & Rudolph,[25] 1937	M, 36 yrs.	Follow the distal chamber	Right anterior sinus—and "L" coronary artery. Left posterior sinus—"R" coronary artery	Aorta anterior and to the left	None	Patent foramen ovale
32. Anderson, Lillehei & Lester,[26] 1957	M, 16 yrs.	Follow the distal chamber	...	Aorta anterior and to the left	Ventricular septal defect	Patent foramen ovale
33. Fink, Adams, McFall & O'Loughlin,[27] 1958	M, 26 mos.	Both A-V valves had three leaflets	...	Aorta anterior and to the left	Ventricular septal defect	...
34. Kernen,[28] 1958	M, 4 mos.	Follow the distal chamber	"Inverted"	Aorta anterior and to the left	Ventricular septal defect	Patent foramen ovale
35. Kernen,[28] 1958	M, 5 wks.	Follow the distal chamber	"Inverted"	Aorta anterior and to the left	Fetal coarctation with ventricular septal defect	Patent ductus arteriosus
36. Kernen,[28] 1958	F, 3 1/2 mos.	Follow the distal chamber	"Inverted"	Aorta anterior and to the left	Fetal coarctation with ventricular septal defect	Patent ductus arteriosus
37. Novak,[29] 1960	F, 9 days	Follow the distal chamber	...	Aorta anterior and to the left	Ebstein's anomaly of left A-V valve. Atrial septal defect (secundum type)	Patent ductus arteriosus

re-establishment of the absolutely normal course of the circulation, despite abnormal positions of the arterial or venous trunks or the position of chambers.

The cases of mixed levocardia with ventricular inversion and inverted transposition reviewed in the literature reveal the following: (1) the A-V valve corresponds to the distal chamber; (2) the anterior descending coronary artery emerges from the right-sided coronary sinus of Valsalva; (3) the complexes found are: (a) no other abnormalities, (b) isolated ventricular septal defect, (c) pseudotruncus, (d) ventricular septal defect with pulmonary stenosis, (e) left A-V valve insufficiency, (f) coarctation of the aorta, (g) stenosis or atresia of the left A-V valve, and (h) Ebstein's anomaly of the left A-V (tricuspid) valve. Incidental findings are as follows: persistent left superior vena cava draining into the coronary sinus, bicuspid aortic valve, rete chiari, atrial septal defect, patent foramen ovale and patent ductus arteriosus. In addition, the usual shape of the heart was recognized by Rokitansky[4] and Walmsley,[14] the enlarged pars membranacea and the abnormal coronary venous return were emphasized by Walmsley[14] and the abnormal coronary artery distribution by Geipel,[10] Walmsley,[14] Harris and Farber[17] and Anderson, Lillehei and Lester.[26]

From an analysis of the reviewed cases of mixed levocardia with atrial inversion, it is clear that they are all part of one type of isolated levocardia with abdominal situs inversus, and in some cases with inversion of the lungs. Many have splenic abnormalities. All are associated with a transposition complex, often with pulmonary stenosis or atresia, and most with right aortic arch. The systemic veins usually enter the morphologic right (left-sided) atrium and the pulmonary veins the morphologic left (right-sided) atrium. In Platzer's[21] case, however, a small right superior vena cava drained into the morphologic left atrium with the pulmonary veins, a left superior vena cava entered the morphologic right atrium with the coronary sinus and inferior vena cava. In Ivemark's[41] case, the left pulmonary veins joined the systemic veins in the morphologic right atrium. Common associated anomalies are biscuspid or absent pulmonic valve, patent ductus arteriosus and patent foramen ovale. Other anomalies mentioned are absent coronary sinus[42]; inferior vena cava draining into the superior vena cava[8]; and separate hepatic vein draining into the morphologic right atrium.[8]

Nomenclature

The initial problem facing the prosector in diagnosing a heart with mixed levocardia is that of nomenclature. This problem pertains to the appelation of chambers, valves and coronary arteries. As one of us[1] has previously pointed out, chambers cannot be adequately named according to the type of blood they carry or according to their proximal and distal connections. Chambers are best named according to the morphology and morphology is best recognized by the architecture of the septum. The right atrium is that chamber which presents the limbus fossa ovalis. The left atrium is that chamber which presents the derivative of the septum primum. The right ventricle is that chamber which presents the septal and parietal bands forming the crista, and a markedly trabeculated septum in the inlet. The left ventricle is that chamber which presents a relatively nontrabeculated septal surface in its basilar portion, and a mildly trabeculated apical portion, with the fibers streaming parallel to the outflow of blood. It is, therefore, convenient to use the term "morphologic" in referring to the correct anatomic chamber, regardless of its position. At the same time, for clinical correlation, the term "left-sided" or "right-sided" may be added to indicate the actual position of the chamber, regardless of its morphology.

This method of designation, however, does not suffice to equate hypertrophy and dilatation of the ventricles in a hemodynamic sense. The additional use of the terms "venous" ventricle and "arterial" ventricle, denoting the type of blood, would be suitable for mixed levocardia with ventricular inversion and inverted transposition of the arterial trunks, but not necessarily for the other types of mixed levocardia. The terms "pulmonic" and "aortic" ventricle, pertaining to the distal connections of the chamber, could be used hemodynamically for all types of mixed levocardia with the exception of the instance of both vessels coming from the same chamber.

Hence, in diagnosing an atrium the morphologic and positional relationships are mentioned. In diagnosing a ventricle, the hemodynamic relationships are referred to, in addition to the factors mentioned, as follows: "hypertrophy (or atrophy) of the morphologic (right-sided) ventricle"; "hypertrophy (or atrophy) of the 'pulmonic' or 'aortic' ventricle." It is thus possible for a ventricle to be the seat

TABLE II

Heart Weights and Measurements (after Fixation) in Thirteen Cases of Mixed Levocardia

Measurement	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11	Case 12	Case 13
Total heart weight (gm.)	573.0	140.0	512.0	468.0	190.0	542.0	168.0	47.0	34.0	193.0	484.0	317.0	21.0
Wall thickness (cm.)													
Right ventricle													
Pulmonic	1.0	0.6	0.9	0.7	0.9	0.9	1.0	0.5–0.6	0.4	0.8	0.7	0.6	0.8
Tricuspid	1.2	0.7	0.9	0.8	0.9	1.0	0.6	0.5	0.4	0.6	1.0	0.8	0.3–0.4
Apex	0.2–0.3	0.3	0.2	0.3	0.3	0.3	0.2	0.2	0.4	0.2	0.1–0.2	0.4	0.1
Left ventricle													
Maximum	0.7	0.7	1.0	1.1	1.2	1.2	0.9	0.6	0.7	0.7	0.7	1.0	0.4
Apex	0.1	0.1–0.2	0.2	0.2	0.2–0.3	0.4	0.3	0.1	0.2–0.3	0.5–0.6	0.3	0.2–0.3	0.1
Circumference of orifice (cm.)													
Right A-V	11.0	6.1	12.1	11.5	6.5	11.0	8.2	5.0	3.5	8.1	9.3	8.0(mitral)	2.3(mitral)
Pulmonic	5.6	3.6	7.0	6.1	4.3	5.9	3.7	...	3.0	4.0	4.7	5.0	1.2
Left A-V	11.0	5.4	12.1	6.5	6.2	9.0	4.5	3.6	3.1	6.5	12.3	10.0(tricuspid)	3.2(tricuspid)
Aortic	6.0	2.4	5.7	5.8	3.9	6.0	5.2	3.0±	1.9	4.7	8.2	4.0	2.5
Internal wall measurements (cm.)													
Right ventricle													
Inlet length	7.0	4.3	6.2	6.3	4.2	7.4	4.1	3.9	2.2	3.6	7.5	5.0	1.9
Inlet perimeter	8.5±	4.0	7.5	5.6	5.0±	7.0	2.0	2.8	2.8	3.0	6.0	4.0	2.1
Outlet length	10.0	4.7	8.5	7.2	5.5	7.9	4.0	4.3±	2.4	4.2	9.8	6.0	3.0
Outlet perimeter	8.5±	4.8	7.5	6.0	4.2	7.5	4.6	3.4	3.1	3.8	10.0	6.5	2.8
Left ventricle													
Inlet length	8.7	6.0	8.5	7.3	6.0	8.0	5.5	2.0	3.1	5.8	6.8	6.6	2.5
Outlet length	10.0	6.0	8.5	8.3	6.0	8.2	5.8	3.1	3.1	6.8	9.0	8.7±	3.8
Perimeter	11.5	7.5	12.5	14.0	7.5	13.5	7.5	4.0	3.9	8.2	12.0	10.0	2.2

TABLE III
Clinical Details of Thirteen Cases of Mixed Levocardia

Case No.	Cyanosis	Cardiac Murmurs	Electrocardiographic Data	X-ray Findings	Catheterization Data	Surgical Findings
1	None	Loud, harsh systolic murmur maximal at apex; middiastolic apical murmur added later	Left axis deviation; episodes of nodal rhythm and atrial arrhythmia; myocardial damage	Cardiomegaly; enlarged left atrium	Mild pulmonary hypertension; no shunts found	...
2	None	Grade 2 apical systolic murmur	Varying 2:1 to 3:1 A-V block at 2 months of age, later becoming complete	Cardiomegaly	...	...
3	None	Marked apical systolic murmur	Left axis deviation; atrial fibrillation; incomplete left bundle branch block	Cardiomegaly; large right atrium and possible tricuspid stenosis	...	Exploratory thoracotomy only
4	Yes	Grade 4 harsh, pansystolic murmur at midleft sternal border; grade 2–3 middiastolic rumble at left lower sternal border	Right ventricular hypertrophy; complete right bundle branch block	Cardiomegaly; increased pulmonary vascular markings	Large L → R shunt at ventricular level; patent ductus arteriosus (?); severe pulmonary hypertension; slightly increased pulmonary vascular resistance	Ventricular septal defect closed using patch; lived 6 weeks
5	Yes	Grade 4 systolic murmur and thrill maximal at left sternal border; grade 3 middiastolic apical rumble	Right heart strain; incomplete right bundle branch block	Cardiomegaly	Large L → R shunt at ventricular level; corrected transposition of the great vessels (?); pulmonary hypertension	Ventricular septal defect closed using patch; lived 2 days
6	Yes	Loud, systolic murmur and thrill at midleft sternal border; grade 2 middiastolic rumble	Right ventricular hypertrophy; first degree A-V block	Cardiomegaly	Large L → R shunt at ventricular level; valvular or subvalvular pulmonic stenosis; corrected transposition of great vessels	Ventricular septal defect closed with a patch; mild valvular pulmonary stenosis corrected under direct vision; lived 41 days

Case No.	Cyanosis	Cardiac Murmurs	Electrocardiographic Data	X-ray Findings	Catheterization Data	Surgical Findings
7	Circumoral and of fingers and toes	Grade 4 harsh systolic murmur and thrill over the second left interspace; separate grade 3 rough systolic murmur at lower left sternal border	Right atrial enlargement; right ventricular hypertrophy	Cardiomegaly; right ventricular hypertrophy	Bidirectional shunt at ventricular level; catheter could not be made to enter pulmonary trunk	Ventricular septal defect closed with a patch; infundibulectomy performed; stenotic pulmonic valve stretched; died at end of operation
8	Yes	Grade 3 systolic murmur in third left intercostal space	Sinus rhythm; right ventricular hypertrophy	Normal	...	Left pulmonary artery anastomosed to aorta; patient too ill to proceed; lived 1 hour
9	Generalized, maximal on face	Harsh systolic murmur maximal in third intercostal space on both sides of the sternum	...	Cardiomegaly; exaggeration of the aortic arch	...	...
10	Yes	Grade 2–3 blowing systolic murmur maximal at apex	Complete A-V block; right heart strain; right atrial hypertrophy (?)	Borderline cardiomegaly	...	Blalock-Hanlon procedure at $2^1/_2$ years of age; modified Baffes procedure; lived 1 day
11	Yes	Grade 4 loud harsh systolic murmur maximal at second right interspace	Right ventricular hypertrophy; delayed left ventricular conduction	Decreased pulmonary vascularity suggestive of pulmonary stenosis; stomach bubble on right; right aortic arch	Catheter introduced into left basilic vein entered left superior vena cava and inferior vena cava; pulmonary hypertension	Ventricular septal defect sutured; infundibular and valvular pulmonary stenosis corrected under direct vision; lived 6 weeks
12	Yes	Grade 4 harsh systolic murmur maximal at fourth left interspace. Apical middiastolic murmur	Marked left ventricular strain	Cardiomegaly; slight right atrial hypertrophy; increased pulmonary vascular markings	Bidirectional shunt at the ventricular level; severe pulmonary hypertension	...
13	Yes	Grade 4 harsh systolic murmur maximal at second right interspace with grade 2 palpable thrill	...	Normal	...	...

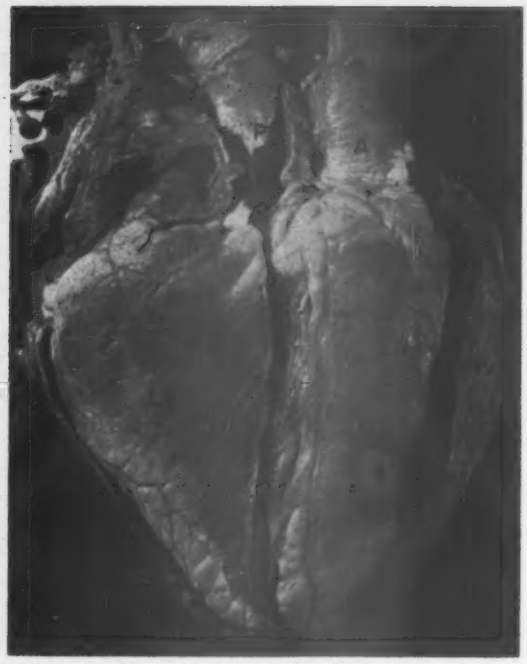


FIG. 1. Case 1. Anterior surface of heart. A = aorta; P = pulmonary trunk; LV = morphologic left ventricle; RV = morphologic right ventricle.

of hypertrophy from the point of reference of morphology, and atrophy from the point of reference of hemodynamics, or vice versa.

The atrioventricular valves are best named according to their morphology as follows: the tricuspid valve is that valve which has papillary muscle and chordal connections reminiscent of the normal tricuspid valve; that is, an anterolateral papillary muscle connected to the anterior and inferior leaflets, a conal band (muscle of Lushka or Lancisi) connected to the anterior and medial leaflets, an inferior papillary muscle connected to the inferior and medial leaflets, and chordae connecting the medial leaflet to the septum. The mitral valve is that valve which is connected to an anterior and a posterior group of papillary muscles. The exact delineation of three or two distinct leaflets is not necessarily present.

In judging the hemodynamic changes[43] of both an atrioventricular and semilunar valve, the valve in question must be compared not only with the corresponding normal valve of this age, but also with the opposite A-V or semilunar valve of this age. For in mixed levocardia, the valve may be related to noncorresponding proximal and distal chambers or vessels, as left atrium and right ventricle or right ventricle and aorta, and hence subjected to the hemodynamic forces which ordinarily act in part on *both* A-V or semilunar valves.

The terminology of the coronary arteries is a very difficult problem in mixed levocardia as well as in advanced types of transposition of the arterial trunks. The terms right and left coronary arteries, as applied to the normal distribution of the right and left coronary arteries, are not pertinent because either coronary artery may "steal" branches from the other. Likewise, referring to a coronary artery according to the right or left position of a coronary ostium is fallacious because the coronary arteries in mixed levocardia emerge from the wrong sinuses of Valsalva. The proper method would seem to be the designation according to the embryologic origin of a sinus of Valsalva; that is, the left coronary artery is that artery which emerges from the sinus of Valsalva which is situated clockwise, and the right coronary artery is that artery which emerges from the sinus of Valsalva which is situated counterclockwise to the noncoronary cusp (looking downwards from the aorta into the ventricle). However, this would be very confusing to the surgeon and clinician. Accordingly, we are using the noncommittal term "right-sided" and "left-sided" coronary artery as simply denoting the definitive positions of the coronary arteries, regardless of their ostial location and the parts of the heart they supply.

REPORT OF CASES

The thirteen cases were studied grossly, equating sizes of chambers and thickness of wall according to a method described elsewhere.[44] The values for these measurements are contained in Table II. The clinical data are summarized in Table III.

CASE 1.* MIXED LEVOCARDIA WITH VENTRICULAR INVERSION, LEFT A-V VALVE (TRICUSPID) INSUFFICIENCY

Clinical Summary: This fourteen year old Negro boy was admitted to La Rabida Sanatorium on July 4, 1958, for the second and last time after repeated admissions to another hospital for chest pain, cough and dyspnea during the previous six months. His first admission to this sanatorium had been in 1949 when he was six years of age. At that time he had tonsillitis, orthopnea, epigastric pain, nausea and pain in both knees and ankles. His heart was enlarged. There was a low-pitched, harsh systolic murmur heard best at the apex, a loud pulmonary second sound and a middiastolic apical murmur. Myocardial ab-

* A brief statement of the pathology of this case has been presented as a CPC in: *Am. Heart J.*, 60: 464, 1960.

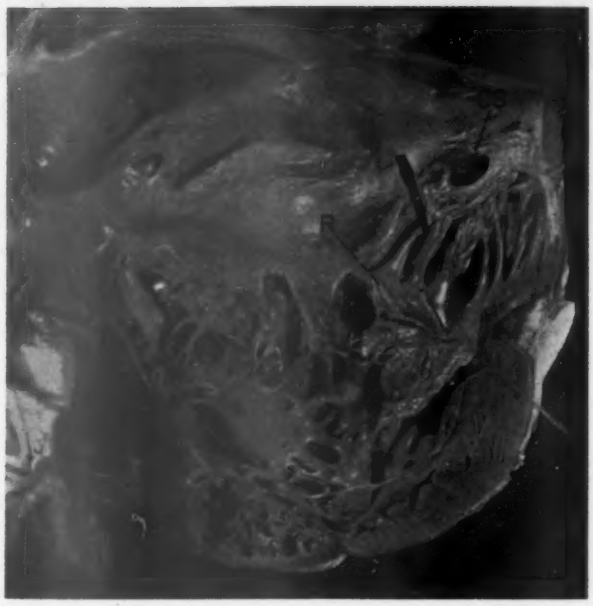


FIG. 2. Case 1. Internal view of left atrium, left-sided A-V (tricuspid) valve and inflow tract of morphologic right (left-sided) ventricle. CS = entry of coronary sinus; R = ridge produced by hemodynamic alteration.

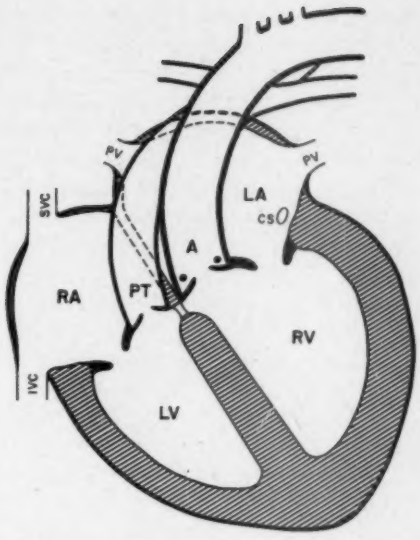


FIG. 3. Case 1. Diagrammatic sketch of the heart. RA = right atrium; RV = right ventricle; LA = left atrium; LV = left ventricle; PT = pulmonary trunk; A = aorta; SVC = superior vena cava; IVC = inferior vena cava; PV = pulmonary veins; CS = coronary sinus.

normalities and left axis deviation were seen on electrocardiography. Repeated throat cultures were negative for beta hemolytic streptococci. He responded to penicillin, aspirin, digitalis and mercury compounds and in July 1950 was discharged on "full activity." For the next eight years he attended school but did not participate in games. His heart size and auscultatory findings did not change. His last admission was characterized by increased respiratory difficulty and cardiac arrhythmia resistant to digitalis therapy. His heart was relatively much larger than in 1950, the point of maximum impulse being in the fifth intercostal space in the anterior axillary line. There was an apical systolic thrill and murmur and a grade 2 diastolic murmur. His liver was enlarged. At first his lungs were clear but later dullness and diminished breath sounds developed in the right side of the chest. He responded a little to treatment but for the last three weeks of his life his course was steadily downhill with abdominal pain, vomiting, hemoptysis and labored asthmatiform breathing. He died in acute respiratory distress in November 1958, three months after admission.

Postmortem Examination: Aside from the findings in the heart the pathologic diagnosis was as follows: (1) chronic passive hyperemia of the lungs with fibrosis; (2) mild hypertrophy of the muscular pulmonary arteries; (3) hyperplastic intimal sclerosis of the pulmonary arterioles and venules; (4) organizing infarct of lung (upper right lobe) with focal fibrinous pleuritis; (5) chronic passive hyperemia of the liver; (6) multiple accessory spleens; and (7) heterotopic pancreatic ducts.

Heart (*Figs. 1, 2, 3*). The heart was enlarged. It was triangular in shape, the broad diameter being less than the longitudinal diameter. The apex was formed by both ventricles. The left margin was more rounded than usual. From the base two arterial trunks of about equal size emerged; one situated to the left and slightly anteriorly and the other to the right and slightly posteriorly. The anterior vessel was identified as the aorta. The anterior descending coronary artery emerged from between the two great vessels on the right side and ran in a more or less straight line from base to apex over the anterior aspect of the heart. The atrial appendage on the right was in the usual position. The atrial appendage on the left could not be seen on the anterior aspect of the heart. The epicardium over the left atrium was markedly granular and thickened. This thickening did not involve the right atrium or the ventricles, but did extend to the adjacent aorta and slightly toward the pulmonary trunk as well.

The mutual relationships of the various chambers were as follows: the right atrium was in its usual position on the right. It communicated with the morphologic left ventricle which was situated anteriorly and to the right. The left atrium was in its usual position on the left. It communicated with the morphologic right ventricle, which was situated posteriorly and to the left.

The right atrium was smaller than the opposite atrium in this heart, but larger than normal for a subject this age. Its wall was thinner than that of the left atrium in this heart, but thicker than the normal right atrium for this age. It received the superior and inferior venae cavae in a normal manner. The coronary sinus did not enter this chamber; instead, there was a blind circular depression resembling the

orifice of the coronary sinus in shape and position. The eustachian valve was normal, but attached a little low on the limbus. There was no thebesian valve. The limbus was well formed but described a wide arc. The foramen ovale was obliquely patent to the extent of about 1 cm. The endocardium of the septal surface was thickened and geographic. The right atrium communicated with the morphologic left ventricle by way of an orifice identified as the mitral orifice. It was the same size as the opposite atrioventricular orifice in this heart, but larger than a normal mitral or tricuspid orifice of a subject this age. The valve was composed of two leaflets having the typical configuration of the anterior and inferior leaflets of a mitral valve. This valve showed increased hemodynamic change as compared to the normal tricuspid valve, and about the same hemodynamic change as a normal mitral valve for this age. The anterior and posterior papillary muscles were within normal limits in position and attachment but were more delicate than is usual.

The morphologic left ventricle was smaller than the opposite ventricle in this heart. It was larger than a normal left ventricle of a subject this age. Its wall was thinner than that of the opposite ventricle, and thinner than that of a normal left ventricle but thicker than that of a normal right ventricle of this age. The pars membranacea was larger than is normal, and in consequence the outflow tract appeared to be more sharply demarcated from the inflow tract than is usual in a left ventricle. The ventricular septum was intact. The endocardium of the outflow tract, particularly over the pars membranacea, was thickened and opaque. From this chamber emerged the pulmonary trunk. The pulmonic orifice was slightly smaller than the aortic orifice in this heart. It was normal in size for a pulmonic orifice of a subject this age. The pulmonic valve was normally formed, and showed slightly increased hemodynamic change as compared to a normal pulmonic valve for this age, and about the same degree of hemodynamic change as compared to a normal aortic valve of a subject this age. The wall of the pulmonary trunk was thinner than that of the aorta but thicker than normal. The main trunk ascended alongside and parallel to the aorta without the usual mutual twisting of these vessels. It gave rise to the main pulmonary arteries in the usual manner. The ductus arteriosus was closed.

The left atrium was tremendous, being larger than the right atrium in this heart, and much larger than a normal left atrium in a subject this age. Its wall was thicker than that of the right atrium, and thicker than that of a normal left atrium. It received the four pulmonary veins in a normal manner. In addition, it received the coronary sinus which entered through the posterior wall of the atrium. The orifice of the sinus was circular and was surrounded by a remarkable serpiginous arrangement of endocardial and myocardial fibers (Fig. 2). The atrial wall was much thicker in this region than elsewhere. The endocardial lining of the posterior wall of the atrium was thrown into folds and ridges in the region of the annulus and was markedly geographic over the fibers of the septum primum as it adhered to the septum secundum. This chamber communicated with the morphologic right ventricle by way of an orifice identified as the tricuspid orifice. This orifice was the same size as the opposite atrioventricular orifice in this heart, and larger than a tricuspid or mitral orifice of a normal subject this age. The leaflet structure of the valve was in general characteristic of a tricuspid valve. The medial leaflet was bifid. There was a marked irregular thickening of the line of closure of the leaflets so that parts were very bulky and granular with relatively thick chordae, and others were thin and apparently eroded. Thus, this valve presented markedly increased hemodynamic change as compared to the normal mitral valve, and immensely increased hemodynamic change as compared to the normal tricuspid valve for this age. The anterolateral and inferior groups of papillary muscles were hypertrophied, in particular the anterolateral group.

The morphologic right ventricle was larger than the opposite chamber, and larger than a right ventricle usual for subjects of this age group. Its wall was thicker than that of the opposite ventricle in this heart, and thicker than that of a normal right or left ventricle of this age. The crista supraventricularis was formed mostly by the septal band; the parietal band was hypertrophied. The endocardium was diffusely thickened throughout the right ventricle. From this chamber emerged the aorta. Its orifice was larger than that of the pulmonary trunk in this heart. It was larger than a normal aortic orifice of a subject this age. The aortic valve was normally formed. All three cusps were irregularly thickened except for the edge of both septal cusps which were fenestrated. Thus, the aortic valve showed slightly increased hemodynamic change as compared to a normal aortic valve for this age, and considerably increased hemodynamic change as compared to a normal pulmonic valve for this age group. The coronary ostia were given off from the posterior and right anterior sinuses of Valsalva. The wall of the aorta was slightly thicker than that of the pulmonic trunk, but it was of about normal thickness for a subject this age. The ascending aorta appeared to be smaller than normal for this age. The brachiocephalic arteries were given off normally. There was a left aortic arch.

The right-sided coronary artery arose from the right anterior sinus of Valsalva. It gave off the anterior descending artery and continued as the right circumflex artery. The left-sided coronary artery arose from the posterior sinus of Valsalva. It formed the left circumflex and supplied branches to the posterior aspect of the heart including the posterior descending artery. The anterior descending coronary vein joined an irregular array of venous channels draining the obtuse margin of the heart, part of the anterior

and the whole of the posterior aspect of the morphologic right ventricle. The common vein so formed ran over the posterior aspect of the left atrium to enter the left atrium about 4 cm. above the level of the tricuspid orifice.

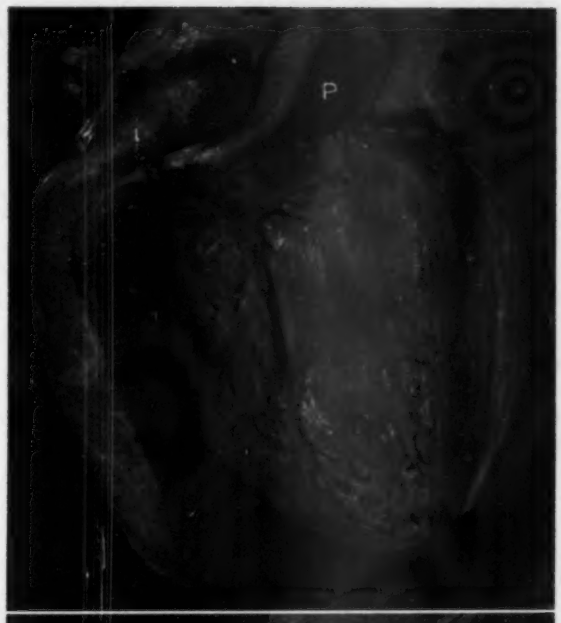
Anatomic Diagnosis:

I. Mixed levocardia (atria normal, ventricles inverted)
II. Complete inverted transposition of the great vessels
III. Insufficiency of the left atrioventricular (morphologic tricuspid) valve complex
  A. Hypertrophy and dilatation of the right atrium
  B. Atrophy and dilatation of the morphologic left (right-sided) ventricle (hypertrophy and dilatation of the pulmonic ventricle)
  C. Marked hypertrophy and dilatation of the left atrium
  D. Hypertrophy and dilatation of the morphologic right (left-sided) ventricle (hypertrophy and dilatation of the aortic ventricle)
  E. Hypertrophy of the wall of the pulmonary trunk
  F. Patent foramen ovale
IV. Entry of the coronary sinus into the left atrium
V. Epicardial thickening of the left atrium

CASE 2. MIXED LEVOCARDIA WITH VENTRICULAR INVERSION, CORRECTED TRANSPOSITION OF ARTERIAL TRUNKS, COARCTATION OF AORTA WITH AORTIC STENOSIS

Clinical Summary: This twenty-two month old white boy was first seen at the Children's Memorial Hospital on March 6, 1954, at the age of two months. At that time he was suffering from an infection of unknown origin and on examination was found to have a pulse rate of 60 to 70 beats per minute, a moderately enlarged heart and a grade 2 apical systolic murmur. The femoral pulses were palpable. An electrocardiogram revealed a varying 2:1 to 3:1 atrioventricular block. His infection responded to penicillin and he was discharged home with a diagnosis of ventricular septal defect with a variable A-V block. An electrocardiogram taken six months later showed complete A-V block which persisted. The femoral pulses at this time had disappeared. He was readmitted in cardiac failure, with or without bronchopneumonia, on five subsequent occasions during the next twenty months. He died in acute respiratory distress on November 17, 1955, three days after having been discharged from the hospital.

Postmortem Examination: Aside from the findings in the heart, the pathologic diagnosis was: (1) pulmonary vascular sclerosis; (2) chronic passive congestion of lungs, liver and kidneys; (3) thymic atrophy.



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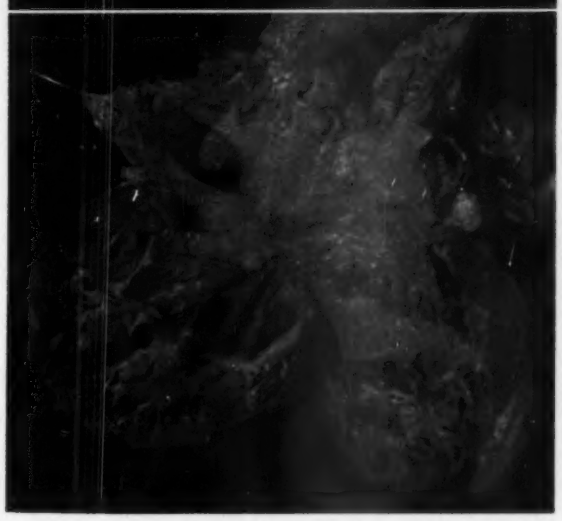

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FIG. 4. Case 2. Internal septal view of the outflow tract of the morphologic left (right-sided) ventricle. A = aorta; P = pulmonary trunk.

FIG. 5. Case 2. Internal view of the left atrium, the left A-V (tricuspid) valve and the inflow tract of the morphologic right (left-sided) ventricle.

Heart (*Figs. 4, 5, 6*). The heart was enlarged and globular in shape. The apex was formed by both ventricles. From the base two arterial trunks emerged, a larger situated posteriorly and to the right, and a smaller anteriorly and to the left. The anterior vessel was identified as the aorta. The anterior descending coronary artery emerged from between the two efferent vessels on the right side. It descended over the anterior surface of the heart from base to apex in a straight line. The atrial appendage on the right was anterior to the pulmonary trunk. The atrial appendage on the left was posterior to the aorta so that only its top could be seen on the anterior aspect of the heart.

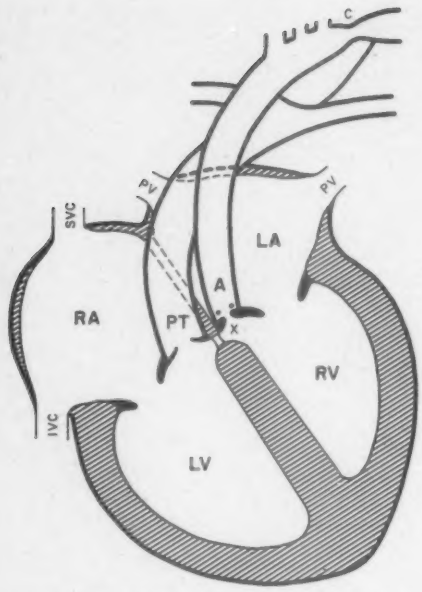

FIG. 6. Case 2. Diagrammatic sketch of the heart. C = coarctation; X = aortic stenosis; other labels as in Figure 3.

The mutual relationships of the various chambers were as follows: the right atrium was in its usual position. It communicated with the morphologic left ventricle which was situated to the right and somewhat anteriorly. The left atrium was in its normal position. It communicated with the morphologic right ventricle which lay to the left and posteriorly.

The right atrium was slightly larger than the opposite atrium in this heart, and larger than normal. Its wall was thinner than that of the opposite atrium but was thicker than normal. The endocardium was thickened and whitened. This chamber received the superior and inferior venae cavae and coronary sinus in a normal manner. The coronary sinus drained a persistent left superior vena cava. The eustachian valve was normally formed; the thebesian valve was not identified. The limbus fossa ovalis was normally formed. There was a valvular patency of the foramen ovale measuring about 0.3 cm. in maximum dimension. This chamber communicated with the morphologic left ventricle by way of an orifice identified as the mitral orifice. This orifice was larger than the opposite atrioventricular orifice in this heart. It was larger than a normal mitral orifice and about the same size as a normal tricuspid orifice of a subject this age. The right atrioventricular valve was composed of an anterior and an inferior leaflet. This valve showed increased hemodynamic change as compared to the normal tricuspid valve and also as compared to the mitral valve of this age. The anterior and inferior leaflets were attached to a smaller group of inferior papillary muscles and to a larger group of anterior papillary muscles.

The morphologic left ventricle was larger than the opposite ventricle in this heart and larger than a left ventricle in a normal heart of this age. Its wall was of the same thickness as that of the opposite ventricle. It was thicker than the wall of a normal right ventricle but of about average thickness for a left ventricle of a subject this age. Its endocardium was diffusely thickened. The interventricular septum was intact (Fig. 4). The pars membranacea was in part composed of muscle. From this chamber emerged the pulmonary trunk. The pulmonary orifice was larger than the aortic orifice in this heart. It was normal in size for this age group. The pulmonary valve was normally formed. All three cusps showed marked hemodynamic change as compared to a normal pulmonic valve and moderately increased hemodynamic change as compared to a normal aortic valve of this age. The wall of the pulmonic trunk was of about the same thickness as that of the aorta in this heart, and was slightly thicker than that of the normal pulmonic trunk. It gave off the two main pulmonary arteries in the usual manner. The ductus arteriosus was closed.

The left atrium was slightly smaller than the opposite atrium in this heart. It was larger than a normal left atrium of this age. Its wall was thicker than that of the right atrium and thicker than normal limits. The endocardium was markedly thickened, whitened and geographic. This chamber received the pulmonary veins normally. It communicated with the morphologic right ventricle by way of an orifice identified as the tricuspid orifice. This orifice was smaller than that of the opposite atrioventricular orifice in this heart. It was of about average size for a normal tricuspid orifice but larger than a normal mitral orifice of this age. The tricuspid valve was composed of an anterior and a fused inferior and medial leaflet. The anterior leaflet was attached to an irregular group of anterolateral papillary muscles and by chordae to the septum. The whole of the inferomedial leaflet was attached directly to the septum by chordae except the most inferior portion which was attached to a short inferior papillary muscle. The attachment of the central portion of this common leaflet was displaced caudally from the true position of the tricuspid orifice. This displacement was insufficiently marked to diminish the size of the tricuspid orifice by more than 1 to 2 mm. There was marked thickening and nodularity of the edge of both leaflets, indicating increased hemodynamic change beyond that of a mitral or tricuspid valve of a subject this age.

The morphologic right ventricle was smaller than the opposite ventricle in this heart. It was of about average size for a right ventricle of a normal subject this age. Its wall was of the same thickness as that of the left ventricle in this heart. It was thicker than the wall of the normal right ventricle, but of about average thickness for a normal left ventricle. The septal band of the crista was markedly hypertrophied. The parietal band was flattened. They joined together to form a narrow crista. The endo-

cardium of this chamber was diffusely thickened. From this chamber emerged the aorta. The aortic orifice was smaller than the pulmonary orifice in this heart and smaller than normal limits. The aortic valve was abnormal. Although it consisted of three cusps, these cusps were attached to each other by high raphés and the sinuses of Valsalva were shallow. The cusps showed marked hemodynamic change as compared to a normal aortic valve of a subject this age, and markedly increased hemodynamic change as compared to a normal pulmonic valve of this age. The coronary ostia arose from the posterior and right anterior sinuses of Valsalva. The wall of the aorta was of the same thickness as the pulmonary trunk in this heart, and thinner than normal. The innominate and left common carotid arteries were distinctly narrowed up to the ligamentum arteriosum. Just proximal to the ligamentum there was a sharp ridge of marked narrowing. The subclavian artery was given off from the middle of the narrowed portion of the transverse aorta.

The right-sided coronary artery arose from the right anterior sinus of Valsalva. It divided into three branches; one branch divided to form the anterior descending coronary and a branch to the conus of the morphologic right ventricle; a second branch ran to the right forming the right circumflex; and there was a third small intermediate branch. The left main coronary artery arose from the posterior sinus of Valsalva. It formed the left circumflex artery which gave off the posterior descending coronary artery and continued in the posterior atrioventricular groove to supply the posterior aspect of the morphologic right ventricle. It ended in a branch which supplied the acute margin of the heart. The anterior descending vein joined vessels from the anterior surface of the morphologic left ventricle, and entered the right atrial appendage by a single orifice. The posterior descending vein entered the coronary sinus together with a persistent left superior vena cava.

Anatomic Diagnosis:

I. Mixed levocardia (atria normal, ventricles inverted)
II. Complete inverted transposition of the arterial trunks (corrected)
III. Coarctation of the aorta with anatomic aortic stenosis and abnormal left atrioventricular valve
   A. Biatrial hypertrophy and dilatation
   B. Hypertrophy and dilatation of the morphologic left (right-sided) ventricle (hypertrophy and dilatation of the pulmonic ventricle)
   C. Hypertrophy and dilatation of the morphologic right (left-sided) ventricle (normal aortic ventricle)
   D. Patent foramen ovale
IV. Persistent left superior vena cava draining into the coronary sinus

CASE 3. MIXED LEVOCARDIA WITH VENTRICULAR INVERSION, CORRECTED TRANSPOSITION OF THE GREAT VESSELS, COARCTATION OF AORTA AND EBSTEIN'S ANOMALY OF THE LEFT ATRIOVENTRICULAR VALVE

Clinical Summary: This fourteen year old white boy was first admitted to Bob Roberts Hospital in May 1947, at the age of eight years, for investigation of numerous attacks of paroxysmal tachycardia for the preceding year and a half, and exertional cyanosis. On examination, there was anterior bulging of the sternum, a marked systolic thrill and a harsh murmur maximal over the left fifth interspace with a marked precordial thrust. There was also a moderately loud middiastolic murmur heard best at the left sixth interspace and propagated to the axilla. Both femoral pulses were present. The liver and spleen were enlarged. An x-ray film of the chest showed marked cardiac enlargement and an electrocardiogram revealed left axis deviation.

He was readmitted for evaluation of his cardiac status in January 1953 and was referred for surgery in March 1953. On examination he was thin, pale and apparently in chronically ill health. There was well established atrial fibrillation controlled by digitalis to give a ventricular rate of 90 beats per minute. The point of maximum cardiac impulse was now in the seventh interspace between the nipple and axillary lines, with a marked apical systolic thrill and murmur. The liver and spleen were greatly enlarged. An electrocardiogram showed incomplete left bundle branch block. X-ray films showed a grossly dilated right atrium with possible tricuspid stenosis. Exploratory thoractomy was performed on March 9, 1953. There were no lesions amenable to surgery, so the chest was closed and the child was discharged in fair condition. The details of his death in 1958 are not available.

Postmortem Examination: Details of the organs were not available.

Heart (*Figs. 7, 8*). The heart was enlarged. It was bizarre in shape, the upper part of the left border being rounded. The apex was formed by both ventricles. From the base two arterial trunks emerged, a smaller, situated anteriorly and to the left and a larger, situated posteriorly and to the right. The anterior vessel was identified as the aorta. The anterior descending coronary artery emerged from between the two great efferent vessels on the right side. It ran in a more or less straight line over the anterior aspect of the heart from base to apex. The atrial appendage on the right lay between the two efferent vessels on their right aspect. The atrial appendage on the left lay to the left of the posterior efferent vessel. It was displaced caudally and could only be seen on the anterior aspect of the heart. The epicardium was diffusely thickened especially over the anterior aspect of the ventricles.

The mutual relationships of the various chambers were as

FIG. 7. Case 3. Internal view of left atrium, left A-V (tricuspid) valve, and inflow tract of the morphologic right (left-sided) ventricle. Note the Ebstein type malformation of the valve.

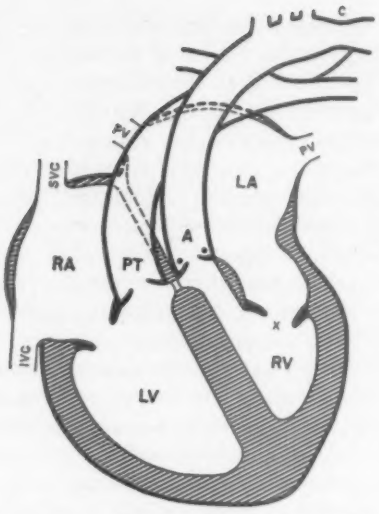

FIG. 8. Case 3. Diagrammatic sketch of the heart. X = displaced left A-V (tricuspid) valve; C = coarctation; other labels as in Figure 3.

follows: the right atrium was in its normal position on the right. It communicated with the morphologic left ventricle which was situated anteriorly and to the right. The left atrium was in its normal position on the left. It communicated with the morphologic right ventricle which was situated posteriorly and to the left.

The right atrium was immense. It was much larger than the normal right atrium but smaller than the left atrium. The wall was thicker than that of the left atrium in this heart and thicker than normal. It received the superior and inferior venae cavae and coronary sinus in the usual manner. The eustachian valve was prominent. The thebesian valve was represented by a single strand of endocardium. The limbus fossa ovalis was well formed. The foramen ovale was obliquely patent to the extent of about 1 cm. in greatest dimension. The endocardium was diffusely thickened. The right atrium communicated with the morphologic left ventricle by way of an orifice which did not have the characteristic appearance of a mitral or tricuspid orifice. It was about the same size as the left atrioventricular orifice in this heart. It was larger than a normal tricuspid orifice and much larger than a normal mitral orifice for a subject this age. The valve was composed of three leaflets. The anterior leaflet was attached to a small papillary muscle arising from the anterior wall of the right-sided ventricle. The inferior leaflet was attached to a group of inferior papillary muscles. The medial leaflet was larger than the other leaflets and lay in the same relationship to the right semilunar valve cusps in this heart as a normal aortic leaflet of the mitral valve to the left semilunar valve cusps. Unfortunately, its connections had been cut and its exact relationship to the papillary muscle groups and septum could not be stated. This valve showed moderately increased hemodynamic change as compared to a normal tricuspid valve and slightly increased change as compared to a normal mitral valve of a subject this age.

The morphologic left ventricle was larger than the opposite ventricle in this heart. It was larger than a left ventricle in a normal heart of a subject in this age group. Its wall was slightly thicker than that of the opposite ventricle in this heart. It was normal in thickness for a left ventricle but much thicker than a normal right ventricle in this age group. The trabeculae carneae and papillary muscles were flattened. The endocardial lining was diffusely but mildly thickened and whitened. The pars membranacea was disproportionately large. The ventricular septum was intact. The pulmonary trunk emerged from this chamber. The pulmonary orifice was larger than the aortic orifice in this heart and larger than a normal pulmonary orifice. The pulmonary valve was normally formed. This valve showed slightly increased hemodynamic change as compared to a normal pulmonic valve, and about the same amount of change as compared to the aortic valve of a normal subject this age. The wall of the pulmonary trunk was thicker than normal, being about the same thickness as the wall of the aorta. The pulmonary trunk gave off the two pulmonary arteries in a normal manner. The ductus arteriosus was closed.

The left atrium was gigantic. It was larger than the right atrium in this heart, and much larger than a left atrium in a heart of a normal subject this age. The dilatation of the main chamber also involved the opening of the atrial appendage and orifices of the pulmonary veins. Its wall was thinner than that of the right atrium in this heart, and of about normal

thickness for this age. It received the four pulmonary veins in a normal manner. The endocardium covering the septal surface was roughened and geographic in outline. The left atrioventricular orifice was the same size as the right atrioventricular orifice in this heart, and was larger than a normal mitral or tricuspid orifice. The left atrioventricular valve was displaced toward the apex. The valve was indistinctly divided into two leaflets. The inferior leaflet was plastered against the inferior wall of the ventricle and anchored there by numerous short chordae, except at its posterior extremity where it was attached to a small group of short papillary muscles. The anterior leaflet was also attached to this group of short papillary muscles and to the septal band of the crista. The free edge of the anterior leaflet was rolled. Both leaflets were irregularly thickened and nodular, particularly in the region of the attachment to the chordae. Thus, the left A-V valve showed markedly increased hemodynamic change as compared to a mitral valve of a normal subject this age, and immensely increased hemodynamic change as compared to a tricuspid valve of this age group. The resulting new orifice formed by the free edges of the valve cusps measured only 1 cm. less than the orifice at the annulus.

The morphologic right ventricle was smaller than the opposite ventricle in this heart but larger than the right ventricle in a normal heart of this age. The wall was slightly thinner than that of the opposite ventricle in this heart. It was thicker than the wall of a normal right ventricle, but thinner than that of a normal left ventricle. The sinus region of this chamber was small and was largely occupied by the abnormally placed left atrioventricular valve. The endocardium was diffusely thickened and whitened. The sinus was sharply divided from the conus by a narrow ridge. This ridge was continuous with the free edge of the inferior leaflet of the left atrioventricular valve and together with it separated inflow and outflow tract. The chamber of the conus was large. Endocardial whitening was also present here but to a lesser extent than in the chamber of the sinus. The crista supraventricularis was formed mostly by a thickened septal band. The parietal band was represented by an irregular network of trabeculae carneae. From the morphologic right ventricle emerged the aorta. The aortic orifice was smaller than the pulmonic orifice in this heart. It was of average size for an aortic orifice of a subject this age. The aortic valve was normally formed. It showed about the same, or somewhat diminished hemodynamic change as compared to a normal aortic valve of this age group, and increased hemodynamic change as compared to a normal pulmonic valve of this age. The sinuses of Valsalva were shallow. The wall of the aorta was the same thickness as that of the pulmonary trunk. It was thinner than normal. There was a left aortic arch. The brachiocephalic arteries were given off normally. The ascending aorta was slightly narrower than normal. After the first brachiocephalic vessel was given off, the arch became much narrower. The next two brachiocephalic vessels arose from the narrow portion. The caliber of the descending aorta was within normal limits.

The right-sided coronary artery arose from the right anterior sinus of Valsalva. It gave rise to the anterior descending coronary artery and to a branch to the anterior aspect of the morphologic left ventricle, and then continued as the right circumflex artery. This artery gave off an atypical branch which ran posterior to the efferent vessels to reach the left atrioventricular sulcus. It lay in the sulcus above the normally placed left circumflex coronary artery (to be described), and terminated in the sulcus. After giving off this branch, the right circumflex artery gave off further branches to the acute margin of the heart, then continued in the atrioventricular sulcus to end as the posterior descending artery. The left coronary artery arose from the posterior sinus of Valsalva. It gave off several small branches to the obtuse margin of the heart, then continued as the left circumflex artery, giving off several branches to the posterior aspect of the morphologic right ventricle. The anterior descending vein, branches from the anterior surface of the morphologic left ventricle and from the acute margin of the heart, formed a sinus which entered the right atrial appendage by way of a single orifice. The posterior descending vein joined veins from the obtuse margin of the heart to form a common vein which entered the right atrium in the usual position.

Anatomic Diagnosis:

I. Mixed levocardia (atria normal, ventricles inverted)
II. Complete inverted transposition of the great vessels (corrected)
III. Coarctation of the aorta
IV. Ebstein's anomaly of the left atrioventricular valve
    A. Right atrial hypertrophy and dilatation
    B. Marked left atrial hypertrophy and dilatation
    C. Hypertrophy and dilatation of the morphologic left (right-sided) ventricle (hypertrophy and dilatation of the pulmonic ventricle)
    D. Hypertrophy and dilatation of the morphologic right (left-sided) ventricle (hypertrophy and dilatation of the aortic ventricle)
    E. Patent foramen ovale
    F. Dilatation of the pulmonary trunk
    G. Hypoplasia of the aorta
V. Chronic epicarditis
VI. Accessory left circumflex coronary artery

FIG. 9. Case 4. Anterior view of the heart. A = aorta; P = pulmonary trunk; LV = morphologic left ventricle; RV = morphologic right ventricle.

CASE 4. MIXED LEVOCARDIA WITH VENTRICULAR INVERSION, CORRECTED TRANSPOSITION OF ARTERIAL TRUNKS, VENTRICULAR SEPTAL DEFECT, LEFT A-V VALVE (TRICUSPID) STENOSIS

Clinical Summary: This thirteen year old white boy was known to have a harsh systolic murmur since the age of four and one half months. His first three years of life were characterized by repeated infections of the upper respiratory tract, recurrent otitis media and poor growth. He was not cyanosed. He attended the cardiac clinic of the Children's Memorial Hospital regularly until the age of twelve years. On admission at that time he was thin, pale and cyanotic with a somewhat bulging precordium. A grade 4 harsh pansystolic murmur was heard at the midleft sternal border and a grade 2 to 3 middiastolic rumble at the left lower sternal border. An electrocardiogram showed complete right bundle branch block and right ventricular hypertrophy. There was gross cardiac enlargement and increased pulmonary vascular markings on the chest roentgenogram. Cardiac catheterization revealed a large left to right shunt at the ventricular level, a probable patent ductus arteriosus, severe pulmonary hypertension and slightly increased pulmonary vascular resistance. Closure of the ventricular septal defect was performed on August 13, 1959. A complete atrioventricular block, with a ventricular rate of about 50 beats per minute, developed after operation. The child was discharged to a nursing home on September 22, 1959, where he died unexpectedly two days later, six weeks after surgery.

Postmortem Examination: Other than the findings in the heart, the pathologic diagnosis was bilateral pulmonary congestion.

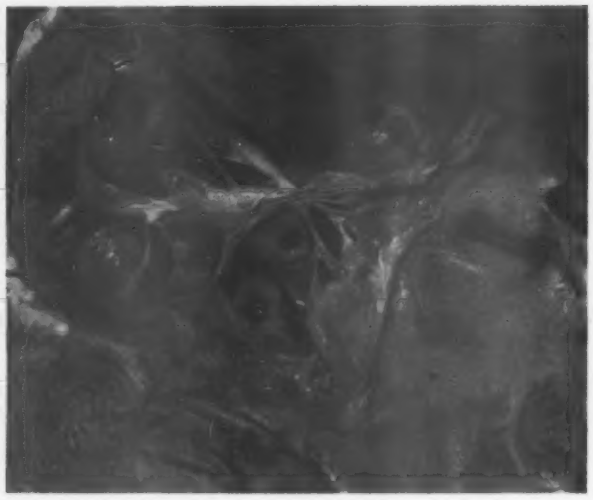

FIG. 10. Case 4. Internal view of left atrium, left A-V (tricuspid) valve, and inflow tract of morphologic right (left-sided) ventricle. Note the left A-V orifice stenosis and abnormal inflow tract of the ventricle.

Heart (Figs. 9, 10, 11). The heart was enlarged. It was bizarre in shape, the left upper border meeting the apex almost at right angles. The apex was formed by both ventricles. From the base two arterial trunks emerged, a smaller, situated anteriorly and to the left and a larger, situated posteriorly and to the right. The anterior vessel was identified as the aorta. The anterior descending coronary artery emerged between the two efferent vessels on the right side and descended over the anterior aspect of the heart in a broad arch convex toward the right, bearing slightly toward the left at the apex. The atrial appendage on the right lay in its usual position. The atrial appendage on the left lay behind the aorta and was just visible on the anterior aspect of the heart.

The mutual relationships of the various chambers were as follows: the right atrium was in its normal position. It communicated with the morphologic left ventricle which was situated anteriorly and to the right. The left atrium was in its normal position. It communicated with the morphologic right ventricle which lay posteriorly and to the left.

The right atrium was slightly larger than the left atrium and larger than normal. Its wall was of about the same thickness as that of the left atrium but was much thicker than normal. This chamber received the superior and inferior venae cavae in the normal manner. The opening of the coronary sinus was enormous. It received a persistent left superior vena cava. The eustachian and thebesian valves were combined into a single band which was attached distal to the coronary sinus and close to the tricuspid valve. The limbus was normally formed. The foramen ovale was closed. The fossa ovalis was redundant and was probably herniated toward one side or the other. The endocardium was focally

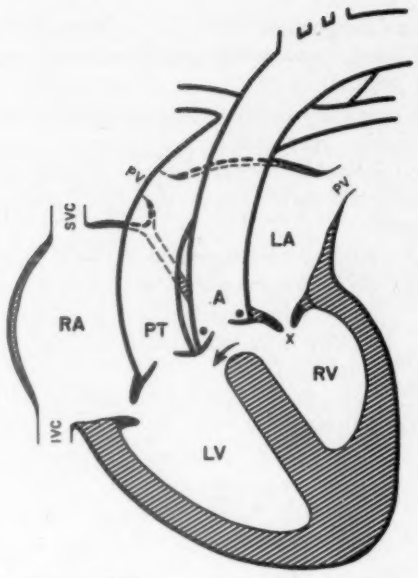

FIG. 11. Case 4. Diagrammatic sketch of heart. X = left A-V (tricuspid) stenosis; other labels as in Figure 3.

thickened. This chamber communicated with the morphologic left ventricle by way of an orifice which was identified as a mitral orifice. It was larger than the tricuspid orifice in this heart, and larger than either a mitral or tricuspid orifice in the heart of a normal subject this age. The leaflet structure of the mitral valve and the position of the papillary muscles was normal, except that the anterior papillary muscle was divided into two separate portions and the posterior papillary muscle was divided into a number of separate units. This valve showed an increased amount of hemodynamic change as compared to a normal tricuspid valve, as well as an increased amount as compared to the mitral valve of a subject this age.

The morphologic left ventricle was larger than the opposite ventricle in this heart and much larger than that of the left ventricle in a normal heart of this age. The wall was slightly thicker than that of the opposite ventricle in this heart. It was thicker than that of a normal right ventricle but thinner than the wall of a normal left ventricle of a subject this age.* The trabeculae carneae and papillary muscles were hypertrophied. There was a large defect measuring 4.3 cm. in greatest dimension in the basal part of the ventricular septum. It involved the posterior part of the anterior septum and the adjacent pars membranacea. The pars membranacea was relatively larger in this heart than in a normal heart of this age. The atrioventricular portion lay between the defect and the mouth of the efferent vessel. The defect entered the morphologic right ventricle between the small sinus region and the lower part of the adjacent conus. The endocardium of the morphologic left ventricle was thickened and whitened throughout, especially at the apex and around the defect. From the morphologic left ventricle emerged the pulmonary trunk. The pulmonary orifice was slightly larger than the aortic orifice and was larger than either the pulmonary or aortic orifice in a normal child of this age. The pulmonary valve was normally formed, but it presented marked hemodynamic change as compared to a pulmonic or aortic valve of a normal subject this age. The wall of the pulmonary trunk was thicker than normal. It was of about the same thickness as the wall of the aorta. The main pulmonary arteries were given off normally. The ductus arteriosus was closed.

The left atrium was smaller than the right atrium, but it was larger than a normal left atrium of this age. Its wall was of the same thickness as that of the right atrium and thicker than a normal left atrium. It received the four pulmonary veins in the usual manner. Its endocardium was diffusely thickened, and over the septal surface was geographic. It communicated with the anatomic right ventricle by way of a bicuspid orifice. This orifice was much smaller than the opposite atrioventricular orifice in this heart. It was smaller than a normal tricuspid orifice and slightly smaller than a mitral orifice of normal subject this age. The tricuspid valve was abnormal. It consisted of a medial and a fused anterior and inferior leaflet. The medial leaflet was connected to the septum by an irregular array of chordae. It did not appear to have the normal mobility of a normal medial leaflet. The fused anterior and inferior leaflets were connected to an abnormal anterolateral papillary muscle and by a few chordae to the inferior wall. This muscle had two components, one of which was attached directly to the anterior wall, and the other, which had three parts, was attached like a tripod to the anterior wall, to the apex, and to the septum. This valve showed increased hemodynamic change as compared to a mitral valve or tricuspid valve of a subject in this age group.

The morphologic right ventricle was smaller than the opposite ventricle in this heart. It was of about the same size as the right ventricle in a normal heart of this age. Its wall was slightly thinner than that of the morphologic left ventricle in this heart. It was thicker than a normal right ventricle but thinner than the wall of a normal left ventricle. Because of the way in which the tricuspid valve was attached to the papillary muscles, the right ventricle appeared to be divided into two parts, an inflow and an outflow portion, separated by the abnormal array of papillary muscles which acted as a lattice between the two parts. The trabeculae of the conus region of the ventricle were hypertrophied. The crista supraventricularis was normally formed. The endocardium of this chamber was diffusely thickened. From the morphologic right ventricle emerged the aorta. The aortic orifice was slightly smaller than the pulmonic orifice in this heart, but was larger than a nor-

* Because of the peculiar shape of this chamber, the measurements in the table do not accurately reflect the thickness of the wall.

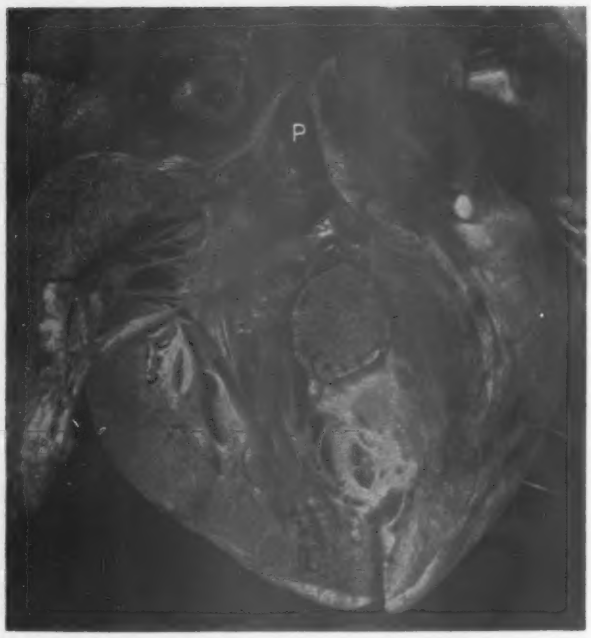

FIG. 12. Case 5. Septal view of morphologic left (right-sided) ventricle. Note muscle bands between mitral valve and septum. A = aorta; P = pulmonary trunk.

mal aortic orifice. The aortic valve was normally formed. It showed about the same amount of hemodynamic change as the normal aortic valve, but less than that of a pulmonic valve of this age. The wall of the aorta was of about the same thickness as that of the pulmonary trunk, but it was slightly thinner than normal. The brachiocephalic vessels were given off normally. There was a left aortic arch.

The right-sided coronary artery arose from the right anterior sinus of Valsalva. It emerged between the root of the aorta and pulmonary trunk. It gave rise to the anterior descending coronary artery. It continued as the right circumflex artery to supply the anterior aspect of the morphologic left ventricle. The left-sided coronary artery emerged from the posterior sinus of Valsalva. It formed the left circumflex artery and ran posteriorly in the atrioventricular sulcus to supply the posterior aspect of the heart. Extensive epicardial thickenings masked the fine details of the coronary artery pattern. The anterior descending vein joined a large vein which ran in the atrioventricular sulcus draining the anterior surface of the morphologic left ventricle and the acute margin of the heart. The common vein so formed ran on the anterior wall of the right atrium, parallel to the pulmonary trunk, and entered the superior vena cava at the point where it entered the right atrium. The posterior descending vein received branches from the obtuse margin of the heart, and entered the large coronary sinus with a persistent left superior vena cava.

Anatomic Diagnosis:

I. Mixed levocardia (atria normal, ventricles inverted)
II. Complete inverted transposition of the arterial trunks (corrected)
III. Ventricular septal defect, overriding aorta, and left A-V (tricuspid) valve stenosis complex
  A. Right atrial hypertrophy and dilatation
  B. Hypertrophy and dilatation of the morphologic left (right-sided) ventricle (hypertrophy and dilatation of the pulmonic ventricle)
  C. Left atrial hypertrophy and dilatation
  D. Hypertrophy of the morphologic right (left-sided) ventricle (atrophy of the aortic ventricle)
  E. Dilatation of the pulmonary artery
IV. Persistent left superior vena cava entering the coronary sinus
V. Surgical intervention (closure of ventricular septal defect)

CASE 5. MIXED LEVOCARDIA WITH VENTRICULAR INVERSION, CORRECTED TRANSPOSITION OF ARTERIAL TRUNKS AND VENTRICULAR SEPTAL DEFECT

Clinical Summary: This two year old white girl was known to have had a cardiac murmur since birth. Growth and development had been normal, and except for cyanosis and shortness of breath on feeding, she had been without symptoms. She was admitted to the Children's Memorial Hospital for investigation on March 26, 1958. On examination, the precordium was bulging and the heart was enlarged. There was a grade 3 middiastolic apical rumble and a grade 4 systolic murmur and thrill maximal at the left sternal border. The liver was enlarged. Cardiac catheterization showed a large right to left shunt at the ventricular level, a possible corrected transposition of the great vessels and pulmonary hypertension. Angiography also suggested a corrected transposition of the great vessels. Open heart surgery was performed on November 26, 1958, at which time a ventricular septal defect was closed by means of a synthetic patch. A complete heart block developed after surgery and although recovery was initially good, the child went into a decline and died on the second postoperative day.

Postmortem Examination: Aside from the findings in the heart, the pathologic diagnosis was: (1) acute pulmonary congestion; (2) bilateral hemothorax.

Heart (*Figs. 12, 13*). The heart was enlarged. It was abnormal in shape. The left border met the apical region almost at right angles. The apex was formed by both ventricles. From the base two arterial trunks emerged, a smaller situated anteriorly and to the left and a larger posteriorly and to the right. The anterior vessel was identified as the aorta. It ascended into the neck parallel with and anterior to the pulmonary trunk. The anterior descending

coronary artery emerged from between the two efferent vessels on the right side. It descended over the anterior surface of the heart in a straight line to the apex. The atrial appendage on the right lay anterior and to the right of the pulmonary trunk. Most of the atrial appendage on the left lay posterior to the aorta, only the tip appearing on the anterior surface of the heart.

The mutual relationships of the chambers were as follows: the right atrium was in its usual position anteriorly and to the right. It communicated with the morphologic left ventricle which also lay anteriorly and to the right. The left atrium was in its usual position posteriorly and to the left. It communicated with the morphologic right ventricle which also lay posteriorly and to the left.

The right atrium was smaller than the left atrium in this heart. It was larger than a normal right atrium of this age. Its wall was thinner than that of the left atrium in this heart, but thicker than that of a normal right atrium of this age. It received the superior and inferior venae cavae in a normal manner. The coronary sinus opened into the atrium at the junction of the posterior wall and atrial septum at a greater distance than usual above the annulus, so that its mouth was confluent with that of the inferior vena cava. There was a combined eustachian and thebesian valve which inserted close to the annulus of the A-V valve. The limbus was well formed but shallow. There was a valvular patency of the foramen ovale measuring 0.3 cm. in maximum dimension. The endocardium of this chamber was diffusely whitened and thickened. This chamber communicated with the morphologic left ventricle by way of an orifice identified as the mitral orifice. This orifice was of about the same size as the opposite atrioventricular orifice in this heart. It was larger than either a mitral or tricuspid orifice in a normal heart of this age. The valve was a typical mitral valve with characteristic leaflet structure and papillary muscle attachments. It showed an increased amount of hemodynamic change as compared to the normal tricuspid valve of a subject this age, and a slightly increased amount as compared to a mitral valve of this age.

The morphologic left ventricle was larger than the opposite ventricle in this heart, and larger than a normal left ventricle of this age. Its wall was thicker than that of the opposite ventricle and thicker than either normal ventricles of this age. Two powerful muscle bands extended from the base to the apex between the septum and mitral valve (Fig. 12). There was a defect in the ventricular septum at the base measuring about 1.6 cm. in maximum dimension. It involved the ventriculoventricular portion of the pars membranacea and the adjacent part of the muscular septum. The atrioventricular portion of the pars membranacea was intact and separated the superior margin of the ventricular defect from the pulmonary orifice. The defect entered the lower part of the conus and adjacent part of the sinus of the morphologic right ventricle excavating the crista supraventricularis. The defect had been closed by a synthetic sponge sewn into place with interrupted sutures. The endocardium of the entire left ventricle was diffusely thickened. From this chamber emerged the pulmonary trunk. Its orifice was larger than the aortic orifice in this heart, and larger than a normal pulmonic orifice of this age. The pulmonic valve was normally formed, but the cusps showed markedly increased hemodynamic change as compared to a normal pulmonic or aortic valve of a subject this age. The wall of the pulmonary trunk was the same thickness as the aorta, and of about normal thickness for a pulmonary trunk of this age. It gave rise to the main pulmonary arteries in a normal fashion. The ductus arteriosus was closed.

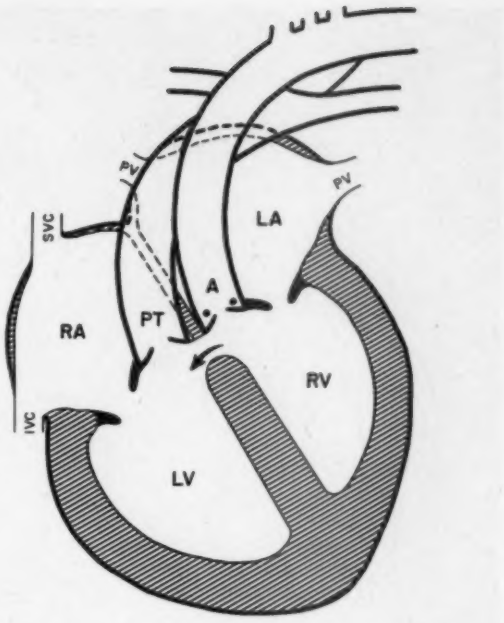

FIG. 13. Case 5. Diagrammatic sketch of heart. Labels as in Figure 3.

The left atrium was larger than the right atrium in this heart and larger than a normal left atrium of this age. Its wall was thicker than that of the right atrium in this heart and thicker than that of a normal left atrium of this age. It received the four pulmonary veins in a normal fashion. Its endocardial lining was thickened and whitened throughout, in excess of normal for this age. This chamber communicated with the morphologic right ventricle by way of an orifice identified as the tricuspid orifice. It was about the same size as the right atrioventricular orifice in this heart. It was normal in size for a tricuspid orifice but larger than a normal mitral orifice of this age. The tricuspid valve was abnormally formed. There was no distinct anterolateral papillary muscle. The anterior leaflet was attached to a hypertrophied muscle of Lancisi and by chordae to the crista supraventricularis. The medial leaflet was attached by chordae to the septum. The

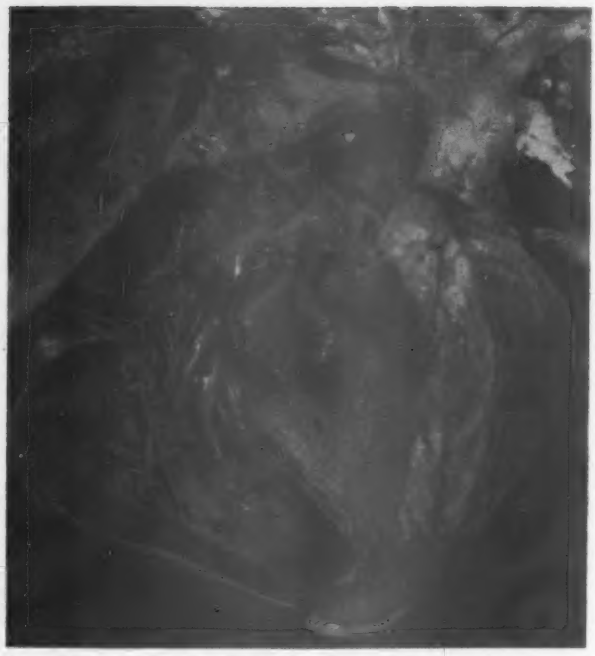

FIG. 14. Case 6. Septal view of morphologic left (right-sided) ventricle. Note ventricular septal defect with prosthesis, abnormal, surgically altered pulmonic valve, and muscle bands between the mitral valve and septum.

inferior leaflet was attached to a group of inferior papillary muscles. All three leaflets were irregularly thickened along the line of closure. The portions of the medial and inferior leaflets related to the defect described above were especially thickened and excavated. Thus this valve showed increased hemodynamic change as compared to the mitral and tricuspid valves of a normal subject this age.

The morphologic right ventricle was smaller than the opposite ventricle in this heart. It was larger than a normal right ventricle of this age. Its wall was thinner than that of the opposite ventricle. It was thicker than that of a normal right ventricle but of average thickness for a normal left ventricle of this age. The crista supraventricularis was normally formed. The endocardial lining was diffusely thickened. From this chamber emerged the aorta. The aortic orifice was smaller than the pulmonic orifice in this heart, but normal as compared to a normal aortic orifice of this age. The aortic valve was normally formed. It showed the usual amount of hemodynamic change as compared to an aortic valve of this age, and an increased amount as compared to the pulmonic valve of this age. The wall of the aorta was the same thickness as the pulmonary trunk in this heart, but thinner than a normal aorta of this age. Four brachiocephalic vessels arose from a left aortic arch.

The right-sided coronary artery emerged from the right anterior sinus of Valsalva. It supplied the anterior descending branch and continued as the right circumflex artery. The left-sided coronary artery emerged from the posterior sinus of Valsalva. It ran to the left as the left circumflex artery. It gave rise to the posterior descending artery. The anterior descending vein joined by veins from the acute margin of the heart to form a common sinus which entered the right atrium by way of two small separate orifices. The posterior descending vein joined branches from the obtuse margin of the heart to enter the coronary sinus in the usual way.

Anatomic Diagnosis:

I. Mixed levocardia (atria normal, ventricles inverted)
II. Complete inverted transposition of the arterial trunks (corrected)
III. Ventricular septal defect complex and abnormal left A-V valve
  A. Biatrial hypertrophy and dilatation
  B. Hypertrophy and dilatation of the morphologic left (right-sided) ventricle (hypertrophy and dilatation of the pulmonary ventricle)
  C. Hypertrophy and dilatation of the morphologic right (left-sided) ventricle (hypertrophy and dilatation of the aortic ventricle)
  D. Hypoplasia of the aorta
  E. Dilatation of the pulmonary trunk
  F. Patent foramen ovale
IV. Surgical intervention (closure of ventricular septal defect)

CASE 6. MIXED LEVOCARDIA WITH VENTRICULAR INVERSION, CORRECTED TRANSPOSITION OF ARTERIAL TRUNKS, VENTRICULAR SEPTAL DEFECT WITH PULMONIC STENOSIS

Clinical Summary: This sixteen and one-half year old white girl was admitted to the Children's Memorial Hospital in April 1959 for cardiac assessment. A cardiac murmur had been noted at the age of two months. Exercise tolerance had been limited in the early years but when seen in 1949 at the age of six years, she was well developed and without symptoms. The heart was moderately enlarged at that time and there was a prominent systolic thrill and loud murmur at the left midsternal border. A grade 2 middiastolic rumble was also heard. The cardiac signs were similar in 1959. The electrocardiogram revealed first degree A-V block and right ventricular hypertrophy. Cardiac catheterization performed on April 14, 1959 showed a large left to right shunt at the ventricular level, valvular or subvalvular pulmonary stenosis and corrected transposition of the great vessels. Open heart surgery was performed on September 23, 1959. The ventricular septal defect was closed with a Teflon patch and a mild valvular pulmonic stenosis was corrected under direct vision. The patient withstood the operation well but a resistant staphylococcal infection later developed at the operative site. She was discharged on the thirteenth postoperative day. Detailed information concerning

her progress at home is not available, but signs of cardiac failure gradually developed and she died on November 4, 1959, six weeks after operation.

Postmortem Examination: Aside from the congenital findings in the heart, the pathologic diagnosis was: (1) localized staphylococcal pericardial abscess overlying right-sided ventriculotomy; (2) right-sided ventricular aneurysm secondary to localized staphylococcal myocarditis; (3) chronic passive congestion of the lungs, liver and spleen; (4) bilateral adhesive pleuritis; (5) mild adhesive pericarditis.

Heart (*Figs. 14, 15*). The heart was enlarged. It was bizarre in shape, the upper part of the left margin meeting the broadened apex almost at right angles. The apex was formed by both ventricles. From the base two arterial trunks emerged, a smaller, situated posteriorly and to the right and a larger, situated anteriorly and to the left. The anterior vessel was identified as the aorta. The anterior descending coronary artery emerged from between the two efferent vessels on the right side and proceeded downwards over the anterior surface of the heart in a more or less straight line until it reached the apex where it swung to the left. The atrial appendage on the right lay in its normal position. The atrial appendage on the left lay behind the anterior efferent vessel and could not be seen on the anterior aspect of the heart.

The mutual relationships of the various chambers were as follows: the right atrium occupied its usual position on the right. It communicated with the morphologic left ventricle which was situated anteriorly and to the right. The left atrium occupied its usual position on the left. It communicated with the morphologic right ventricle which was situated posteriorly and to the left.

The right atrium was smaller than the left atrium in this heart, but was much larger than a right atrium of a normal subject this age. The wall was thinner than that of the left atrium but thicker than normal. It received the superior and inferior venae cavae and coronary sinus in the usual manner. The eustachian valve was prominent. The thebesian valve was represented by a single thin strand bridging the mouth of the coronary sinus. The limbus was indistinct. The foramen ovale was closed. The endocardium was diffusely thickened. The right atrium communicated with the morphologic left ventricle by way of an orifice identified as the mitral orifice. This orifice was larger than the opposite atrioventricular orifice in this heart, and larger than either a normal mitral or tricuspid orifice. The valve was composed of two leaflets having the typical configuration of the anterior and inferior leaflets of the mitral valve. The valve showed increased hemodynamic change as compared to the tricuspid valve of this age, and about the same amount as compared to the mitral valve of this age. The anterior and posterior papillary muscle groups were more broadly based.

The morphologic left ventricle was about the same size as the opposite ventricle, and larger than either ventricle in a heart of a normal subject this age. Its wall was slightly thicker than that of the opposite ventricle in this heart. It was of the same thickness as the wall of a normal left ventricle, but much thicker than that of a normal right ventricle of this age. There were several powerful muscle ridges between the septum and the mitral valve. The endocardium of this chamber was focally thickened throughout. There was a defect in the basal part of the interventricular septum measuring 3.5 cm. in greatest dimension. It involved the interventricular portion of the pars membranacea and the anterior septum adjacent to it. The remaining atrioventricular portion of the pars membranacea lay between the defect and the mouth of the efferent vessel. The defect entered the conus of the right ventricle anterior to the medial leaflet of the tricuspid valve. It excavated the crista to a considerable degree. From the morphologic left ventricle emerged the pulmonary artery. The pulmonary orifice was slightly smaller than the aortic orifice in this heart, and of about average size for this age. The pulmonary valve was bicuspid. There was marked thickening of all parts of both cusps, with a gap between the two cusps on the septal surface. The wall of the pulmonary trunk was thinner than that of the aorta. It was of normal thickness for this age. The pulmonary trunk gave rise to the main pulmonary arteries in the usual manner. The ductus arteriosus was closed.

The left atrium was larger than the right atrium in this heart, and much larger than a normal left atrium of this age. Its wall was tremendously thickened, being thicker than that of the right atrium in this heart, and much thicker than that of a normal left

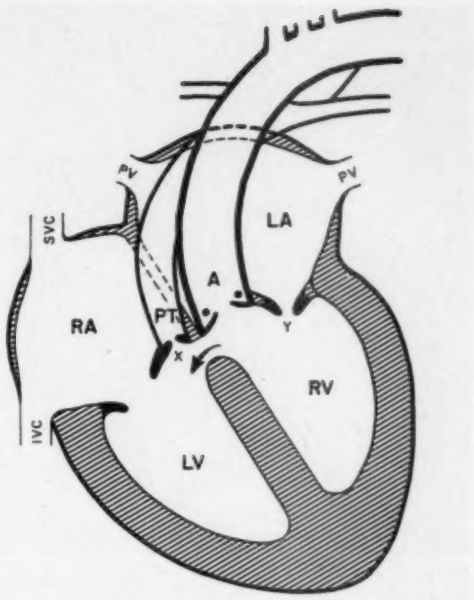

FIG. 15. Case 6. Diagrammatic sketch of heart. X = pulmonic stenosis; Y = left A-V (tricuspid) stenosis; other labels as in Figure 3.

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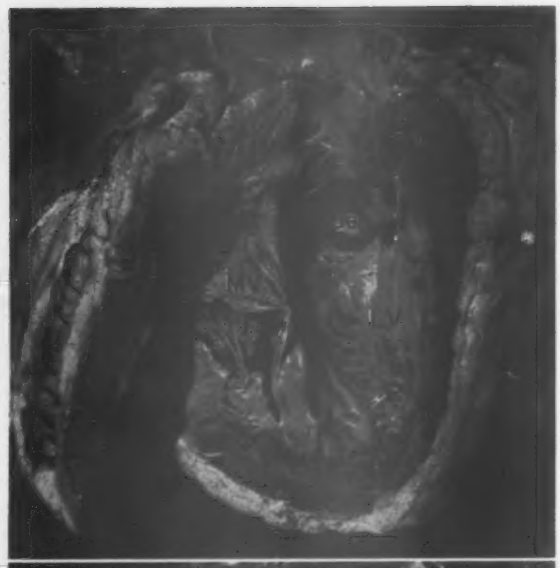

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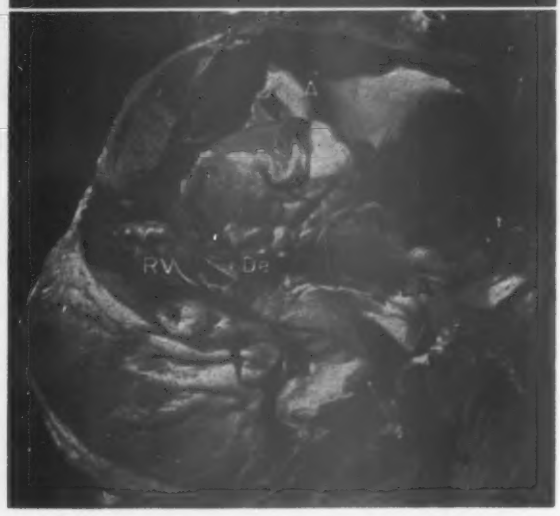

FIG. 16. Case 7. Septal view of morphologic left (right-sided) ventricle. De = defect of ventricular septum with prosthesis partially occluding it; MV = mitral valve; PV = pulmonic valve; R = muscle ridge between septum and mitral valve; LV = morphologic left ventricle.

FIG. 17. Case 7. View of left atrium, left A-V (tricuspid) valve and morphologic right (left-sided) ventricle. A = aorta; RV = morphologic right ventricle; De = defect of ventricular septum; TV = left A-V (tricuspid) valve; LA = left atrium.

atrium. It received the four pulmonary veins in a normal fashion. The endocardium was diffusely whitened and considerably thickened. This chamber communicated with the morphologic right ventricle by way of an orifice identified as the tricuspid orifice. This orifice was smaller than the mitral orifice in this heart, but larger than a normal tricuspid or mitral orifice of this age. The tricuspid valve consisted of three indistinctly divided leaflets. The anterior leaflet was hypoplastic. It was attached to a thin anterolateral papillary muscle. The medial leaflet was attached to the rim of the ventricular septal defect, and at its inferior end by chordae to one of two hypoplastic inferior papillary muscles. The inferior leaflet was also attached by chordae to these small papillary muscles. All three leaflets were markedly thickened and distorted so that their exact identity could not be determined. Thus this valve showed markedly increased hemodynamic change as compared to the normal mitral or tricuspid valve of this age.

The morphologic right ventricle was about the same size as the opposite chamber. It was larger than a normal right ventricle of this age. Its wall was slightly thinner than that of the opposite ventricle. It was much thicker than a normal right ventricle but of about average thickness for a normal left ventricle. The septal and parietal bands of the crista supraventricularis were in their normal position. The crista so formed was excavated by the defect previously described. The endocardium of the whole of the morphologic right ventricle was whitened and thickened, in particular in the region of the anterior wall of the conus. From this chamber emerged the aorta. The aortic orifice was slightly larger than the pulmonary orifice in this heart and was slightly larger than an aortic orifice of this age. The aortic valve was normally formed. It showed increased hemodynamic change as compared to a normal aortic or pulmonary valve of this age. The coronary ostia arose from the posterior and right anterior sinuses of Valsalva. The wall of the aorta was thicker than that of the pulmonary trunk. It was of normal thickness for this age. The brachiocephalic vessels were given off normally. There was a left aortic arch.

The right-sided coronary artery arose from the right anterior sinus of Valsalva. It gave rise to the anterior descending coronary artery and continued on as the right circumflex artery. The left-sided coronary artery arose from the posterior sinus of Valsalva. It formed the circumflex artery which terminated in the posterior descending artery. The detailed pattern of the coronary artery tree was obscured by dense epicardial thickening. The anterior descending vein joined veins from the anterior aspect of the morphologic left ventricle and from the acute margin of the heart to form a common channel which drained into the right atrial appendage by way of one large orifice. The posterior descending vein joined branches from the obtuse margin of the heart to form the coronary sinus which entered the right atrium in the usual manner. The coronary sinus was somewhat smaller than the common channel referred to above.

There was *evidence of surgical intervention* in the epicardium, myocardium and endocardium. The epicardium was diffusely thickened throughout. Over the anterior aspect of the morphologic left ventricle there was considerable dense thickening with the formation of adhesions to the parietal pericardium. The changes over the posterior aspect of the heart were similar but appeared to be more recent. There

were surgical incisions in the right atrial appendage and in the anterior wall of the morphologic left ventricle. In addition, there was an area of necrosis and dilatation in the wall of the morphologic left ventricle adjacent to the suture line. The ventricular septal defect had been closed with a synthetic sponge. The endocardium had begun to grow over the sutures retaining this sponge except in the posterior inferior portion where three sutures had separated from the ventricular wall leaving a defect measuring about 1.5 cm. in greatest dimension.

Anatomic Diagnosis:

I. Mixed levocardia (atria normal, ventricles inverted)
II. Complete inverted transposition of the arterial trunks (corrected)
III. Ventricular septal defect with pulmonic stenosis and abnormal left A-V valve complex
   A. Biatrial hypertrophy and dilatation
   B. Hypertrophy and dilatation of the morphologic left (right-sided) ventricle (hypertrophy and dilatation of the pulmonic ventricle)
   C. Marked hypertrophy and dilatation of the morphologic right (left-sided) ventricle (hypertrophy and dilatation of the aortic ventricle)
   D. Pulmonic valvular stenosis (treated)
   E. Bicuspid pulmonic valve
   F. Dilatation of the pulmonary trunk
   G. Abnormal left atrioventricular (tricuspid) valve
   H. Surgical closure of ventricular septal defect

CASE 7. MIXED LEVOCARDIA WITH VENTRICULAR INVERSION, CORRECTED TRANSPOSITION OF ARTERIAL TRUNKS, VENTRICULAR SEPTAL DEFECT WITH PULMONIC STENOSIS AND OVERRIDING AORTA, STENOSIS OF LEFT A-V (TRICUSPID) VALVE

Clinical Summary: This fourteen year old white girl was first seen in 1945 at the age of fourteen months, when a diagnosis of tetralogy of Fallot was made on the basis of cyanosis and breathlessness on exertion. She was admitted to the University of Illinois Research and Educational Hospitals for cardiac assessment on June 20, 1958. At this time, she was mildly cyanosed and could climb only two flights of stairs without undue breathlessness. Physical examination showed marked circumoral cyanosis and clubbing and cyanosis of the fingers and toes. The point of maximum cardiac impulse was in the fifth left interspace in the midclavicular line. There was a palpable systolic thrill and a grade 4 harsh systolic murmur over the second left interspace. In addition there was a separate, grade 3 rough systolic murmur at the lower left sternal border. Angiocardiography showed simultaneous filling of the aorta and of the right ventricle suggestive of tetralogy of Fallot. Cardiac catheterization demonstrated a bilateral shunt at the ventricular level; the catheter could not be passed into the pulmonary trunk. Open exploratory cardiotomy was performed on October 24, 1958. A basal ventricular septal defect measuring 2.5 cm. was closed with an Ivalon sponge; a small piece of infundibulum was removed and the stenotic pulmonary valve was stretched. The heart started to beat at a normal sinus rhythm but soon went into ventricular fibrillation. Electrical stimulation corrected this but revealed a complete heart block with a ventricular rate of 30 beats per minute. The heart beat gradually became weaker during the closure of the chest and the child died.

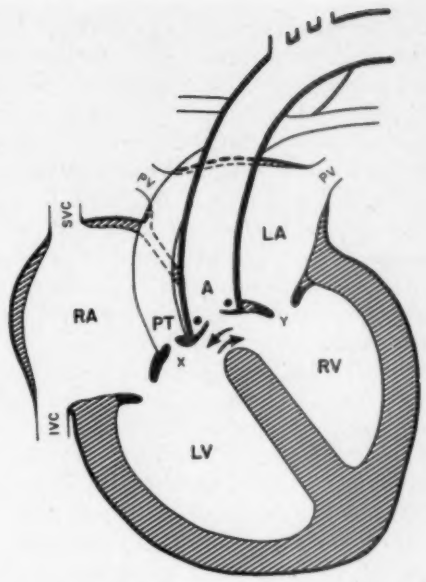

FIG. 18. Case 7. Diagrammatic sketch of heart. X = pulmonary stenosis; Y = left A-V (tricuspid) stenosis.

Postmortem Examination: Aside from the changes in the heart, the pathologic diagnosis was: (1) moderate pulmonary emphysema with marked hyperemia; (2) mild pulmonary arteriosclerosis; (3) acute neuronal degeneration consistent with acute cerebral hypoxia.

Heart (Figs. 16, 17, 18). The heart was bizarre in shape. The longitudinal diameter was greater than the transverse, and greater than normal. There was a pronounced hump on the anterior aspect of the heart at the base of the anterior efferent vessel. The apex was formed by the ventricle on the right. From the base two vessels emerged, a larger situated anteriorly and to the left, and a smaller posteriorly and to the right. The anterior descending coronary artery emerged from between the roots of the great vessels on the right. It started to run downwards in the midline but swung abruptly to the left before reaching the apex. The atrial appendage on the right was in its usual position. The atrial appendage on the left lay behind the aorta and could not be seen on the anterior surface of the heart.

The mutual relationships of the various chambers were as follows: the right atrium was in its normal position. It communicated with the morphologic left ventricle

which lay anteriorly and to the right. The left atrium was in its normal position. It communicated with the morphologic right ventricle which lay posteriorly and to the left.

The right atrium was larger than the left atrium in this heart, but it was of normal size for this age. Its wall was thicker than that of the left atrium in this heart and thicker than that in a heart of a normal subject this age. It received the superior and inferior venae cavae and coronary sinus in a normal manner. There was a common eustachian and thebesian valve. The limbus was poorly defined. The foramen ovale was closed. The endocardium was diffusely thickened. The atrium communicated with the morphologic left ventricle by way of an orifice identified as the mitral orifice. This orifice was larger than the opposite atrioventricular orifice in this heart. It was of normal size for a mitral orifice, and smaller than a normal tricuspid orifice. The mitral valve was normally formed. It showed increased hemodynamic change as compared to the tricuspid valve, and about the same amount as compared to the mitral valve of this age. The anterior and posterior papillary muscle groups consisted of numerous muscles with a broad base of attachment.

The morphologic left ventricle was larger than the opposite ventricle in this heart. It was smaller than a normal left ventricle of this age. Its wall was about the same thickness as that of the opposite ventricle. It was somewhat thinner than a normal left ventricle but thicker than a normal right ventricle of this age. A muscle band extended from base to apex between the septum and the mitral valve (Fig. 16). There was a defect in the basal part of the ventricular septum measuring 2.3 cm. in maximum dimension. It involved the ventriculoventricular part of the pars membranacea and the adjacent part of the muscular septum. The atrioventricular portion of the pars membranacea was intact, and separated the margin of the defect from the mouth of the pulmonary trunk. The defect entered the morphologic right ventricle between the conus and the sinus; it had been partially closed by a synthetic sponge patch. The endocardium of the morphologic left ventricle was irregularly thickened over the apices of the papillary muscle groups and in the subpulmonic region. From this chamber emerged the pulmonary trunk. Its orifice was smaller than that of the aorta in this heart and smaller than normal. The pulmonary valve was irregularly divided into two large cusps which were distorted and thickened. The sinuses of Valsalva were shallow. The wall of the pulmonary trunk was thinner than that of the aorta and thinner than normal. It gave rise to the two main pulmonary arteries in the usual manner. The ductus arteriosus was closed.

The left atrium was smaller than the right atrium in this heart and smaller than normal. Its wall was thinner than that of the opposite atrium in this heart, but probably of normal thickness for this age. The endocardium was normal except for a low band of tissue on the anterior wall of the atrium running parallel to, and just above the atrioventricular valve. The left atrium received the four pulmonary veins in a normal fashion. It communicated with the morphologic right ventricle by way of an orifice identified as the tricuspid orifice. This orifice was smaller than the right atrioventricular orifice in this heart. It was smaller than a normal tricuspid or mitral orifice of this age. The tricuspid valve was abnormally formed. All three leaflets were of about the same size. The anterior leaflet was attached to a small anterolateral papillary muscle in such a way as to form a barrier between the inflow and outflow tracts of this chamber. The medial leaflet was attached by chordae to the rim of the ventricular septal defect described above. The inferior leaflet was attached by chordae to the septum and to the posterior wall of the ventricle. There was no inferior papillary muscle. This valve showed about the same amount of hemodynamic change as a mitral valve of this age but an increased amount as compared to a tricuspid valve of this age.

The morphologic right ventricle was smaller than the opposite ventricle in this heart. It was smaller than a normal right ventricle of this age. Its wall was about the same thickness as that of the opposite ventricle. It was thicker in the conus region than a normal right ventricle but about the same thickness as that of a left ventricle of this age. The endocardial lining was thickened in the conus region. The sinus of the morphologic right ventricle was small, and its wall was of about half the thickness of the wall of the conus. Its endocardium was somewhat less thickened than in the conus. The entrance to the conus was narrowed. It was now noted that the conus straddled the ventricular septum over the defect. The crista supraventricularis was normally formed; both septal and parietal bands were hypertrophied. The crista was excavated and deviated by the ventricular septal defect. From this chamber emerged the aorta. Its orifice was larger than the pulmonic orifice in this heart, but of normal size for this age. The aortic valve was normally formed. It showed about the same amount of hemodynamic change as compared to the aortic valve, and increased hemodynamic change as compared to the pulmonic valve of this age. The wall of the aorta was thicker than that of the pulmonary trunk. It was of average thickness for this age. The brachiocephalic vessels were given off normally. There was a left aortic arch.

The right-sided coronary artery arose from the right anterior sinus of Valsalva. It supplied the anterior descending coronary artery, then continued as the right circumflex artery. The left-sided coronary artery arose from the posterior sinus of Valsalva. It formed the left circumflex artery which ended as the posterior descending branch. The anterior descending vein and veins from the anterior aspect of the morphologic left ventricle and from the acute margin

of the heart joined to form a common vein which drained into the right atrial appendage through two small orifices. The posterior descending vein joined branches from the obtuse margin and drained into the right atrium by way of the coronary sinus in the usual manner. One small vein ran from the coronary sinus to the anterior venous system where it anastomosed with one of the branches supplying the morphologic left ventricle.

Anatomic Diagnosis:

I. Mixed levocardia (atria normal, ventricles inverted)
II. Complete inverted transposition of the arterial trunks (corrected)
III. Ventricular septal defect, pulmonic stenosis, overriding aorta, and left A-V valve (tricuspid) stenosis
   A. Right atrial hypertrophy
   B. Atrophy of the morphologic left (right-sided) ventricle (hypertrophy of the pulmonary ventricle)
   C. Hypertrophy of the morphologic right (left-sided) ventricle (atrophy of aortic ventricle)
   D. Ventricular septal defect (surgically treated)
   E. Pulmonic valvular stenosis (surgically treated)
   F. Bicuspid pulmonic valve
   G. Poststenotic dilatation of the pulmonary trunk
   H. Stenosis of the left atrioventricular (tricuspid) valve

CASE 8. MIXED LEVOCARDIA WITH VENTRICULAR INVERSION, COMPLETE INVERTED TRANSPOSITION, OVERRIDING AORTA AND PULMONARY ATRESIA (PSEUDOTRUNCUS)

Clinical Summary: This six month old white male infant was admitted to the Children's Memorial Hospital on March 31, 1959, for investigation of dyspnea and cyanosis since birth. On physical examination there was slight dyspnea and cyanosis of the skin and mucosae. There was a grade 3 systolic murmur in the third left intercostal space. Electrocardiography revealed sinus rhythm and right ventricular hypertrophy in excess of normal for this age. A venous angiocardiogram was performed on April 9 and showed transposition of the aorta with pulmonary stenosis. The infant had several attacks of dyspnea and cyanosis during the next week. An anastomosis between the left pulmonary artery and aorta was performed on April 16, 1959. Following occlusion of the great vessels during the formation of the anastomosis, the heart rate became very slow, and upon completion of the operation, the heart beat was very weak. The patient died one hour after the operation.

Postmortem Examination: Aside from the findings in the heart, the pathologic diagnosis was: (1) marked congestion of the liver, spleen and kidneys; (2) minimal left hemothorax.

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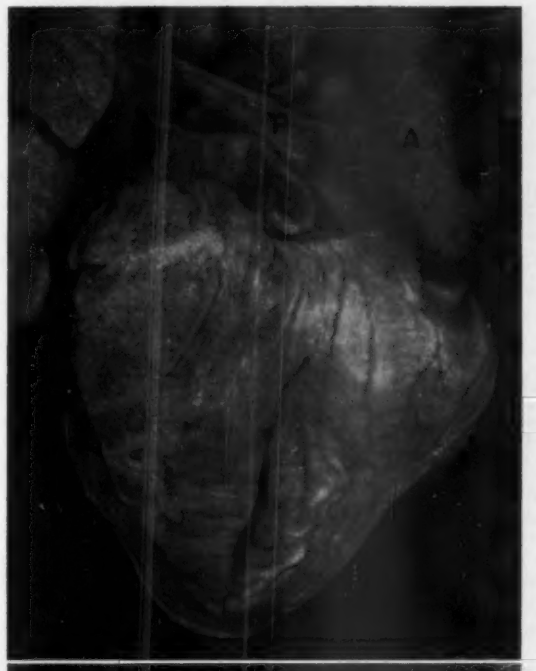

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FIG. 19. Case 8. Anterior surface of the heart. Note that it resembles the normal posterior surface. A = aorta; P = junction of the pulmonary trunk with right pulmonary artery; D = ductus arteriosus.

FIG. 20. Case 8. Septal view of morphologic right (left-sided) ventricle. S = septal band; P = parietal band; A = aorta.

Heart (Figs. 19, 20, 21). The heart was slightly enlarged and triangular in shape. There was a prominent hump on the left anterolateral margin of the heart. The apex was formed by the ventricle lying anteriorly and to the right. From the base two

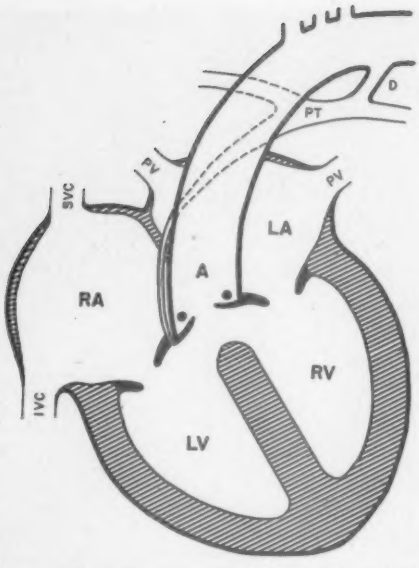

FIG. 21. Case 8. Diagrammatic sketch of heart. D = ductus arteriosus; other labels as in Figure 3.

arterial trunks emerged, a larger, situated anteriorly and to the left and a smaller, situated posteriorly and to the right. The anterior vessel was identified as the aorta. The anterior descending coronary artery arose from between the two efferent vessels on the right and descended over the anterior midline of the heart for about half its course, then swung toward the left. The atrial appendage on the right curved around the anterior efferent vessel. The atrial appendage on the left lay behind the aorta and could not be seen on the anterior aspect of the heart.

The mutual relationships of the various chambers were as follows: the right atrium was in its normal position. It communicated with the morphologic left ventricle which was situated anteriorly and to the right. The left atrium was in its normal position. It communicated with the morphologic right ventricle which was situated posteriorly and to the left.

The right atrium was larger than the left atrium in this heart, and was of about normal size for this age. Its wall was of about the same thickness as that of the left atrium but it was somewhat thicker than normal. The right atrium received the superior and inferior venae cavae and coronary sinus in a normal manner. There was a common eustachian and thebesian valve. The endocardium was diffusely whitened. The limbus was normally formed. There was an oblique patency of the foramen ovale measuring about 0.5 cm. in greatest dimension. The right atrium communicated with the morphologic left ventricle by way of an orifice identified as the mitral orifice. It was larger than the opposite orifice in this heart, but normal in size for a tricuspid orifice and somewhat larger than normal for a mitral orifice of this age. The mitral valve was composed of a normally formed anterior leaflet and a bifid inferior leaflet. It presented about the same hemodynamic change as the normal tricuspid valve and decreased hemodynamic change as compared to the mitral valve. The papillary muscle attachments were normal.

The morphologic left ventricle was the same size as the opposite ventricle in this heart. It was normal in size for a left ventricle of this age. The wall was of about the same thickness as that of the opposite ventricle. It was of normal thickness for a left ventricle, but thicker than a normal right ventricle of this age. The endocardium appeared to be normal. The only outlet from this chamber was through a defect in the basal part of the ventricular septum, corresponding to the site of the pars membranacea and part of the anterior septum adjacent to it. This defect measured 0.8 cm. in maximum dimension. It entered the morphologic right ventricle beneath the crista supraventricularis which was somewhat deviated.

The left atrium was smaller than the right atrium in this heart, and smaller than normal. Its wall was the same thickness as that of the right atrium and was of about normal thickness for this age. It received the four pulmonary veins in the usual manner. The endocardium was grossly normal. It communicated with the morphologic right ventricle by way of an orifice identified as the tricuspid orifice. This orifice was smaller than the mitral orifice in this heart, and smaller than either the tricuspid or mitral orifice in a normal heart. The tricuspid valve was normally formed. It showed increased hemodynamic change as compared to a mitral or tricuspid valve of this age. The papillary muscle attachments were normal.

The morphologic right ventricle was the same size as the opposite ventricle in this heart and normal for a right ventricle of a subject this age. Its wall was the same thickness as that of the opposite ventricle. It was thicker than that of a normal right ventricle and about the same thickness as that of a normal left ventricle of this age. The crista supraventricularis was formed mainly by the septal band which was hypertrophied. This band was deviated anteriorly by the ventricular septal defect described above. The parietal band was in its usual position; it was slightly flattened. It was thus seen that the conus overrode the septum. The endocardial lining over the crista in the region of the defect was somewhat thickened and whitened. From the morphologic right ventricle emerged the aorta. The aortic orifice was slightly larger than a normal pulmonic or aortic orifice of this age. The aortic valve was normally formed. It presented marked hemodynamic change as compared to a normal aortic or pulmonic valve of this age. The wall of the aorta was thicker than that of the pulmonic trunk but thinner than that of a normal aorta of this age. The bracheocephalic vessels were given off normally. There was a left aortic arch. The ductus arteriosus was patent. The pulmonary trunk arose blindly from the base of the heart. There was no pulmonic valve. The trunk lay posteriorly and to the right of the aorta. It gave off the two main pulmonary arteries in the usual way. An end to side surgical anastomosis had been made between the

proximal portion of the left pulmonary artery and the descending aorta below the ductus, which apparently was patent before the operation. In consequence, the left lung after the operation received blood from the bronchial arteries only.

The right-sided coronary artery arose from the right anterior sinus of Valsalva. It gave off the anterior descending artery, then ran in the atrioventricular sulcus as the right circumflex artery. The left-sided coronary artery arose from the posterior sinus of Valsalva. It gave off two small branches to the conus region of the morphologic right ventricle and to the obtuse margin of the heart. It continued in the atrioventricular groove as the left circumflex artery ending as the posterior descending artery. The anterior descending coronary vein joined branches from the anterior aspect of the morphologic left ventricle to form a short common vein which entered the right atrial appendage by a single orifice. The posterior descending vein joined branches from the acute and obtuse margins of the heart and entered the coronary sinus in the usual fashion.

Anatomic Diagnosis:

I. Mixed levocardia (atria normal, ventricles inverted)
II. Complete inverted transposition
III. Overriding conus (aorta) and pulmonary atresia (pseudotruncus) complex
   A. Right atrial hypertrophy
   B. Normal morphologic left ventricle (hypertrophy of pulmonic ventricle)
   C. Hypertrophy and dilatation of the morphologic right ventricle (normal aortic ventricle)
   D. Ventricular septal defect
   E. Patent foramen ovale
   F. Patent ductus arteriosus
IV. Surgical intervention (end to end anastomosis of left main pulmonary artery to descending aorta)

CASE 9. MIXED LEVOCARDIA WITH VENTRICULAR INVERSION, COMPLETE TRANSPOSITION WITH FETAL COARCTATION AND VENTRICULAR SEPTAL DEFECT

Clinical Summary: This four week old male infant was admitted to the Children's Memorial Hospital on September 8, 1945, with a history of respiratory difficulty from birth and intermittent cyanotic spells lasting for about 5 minutes for the past few days. On examination, the baby was well developed and well nourished with striking generalized cyanosis, most marked on the face. The heart was slightly enlarged, the point of maximum impulse being in the fourth intercostal space behind the nipple line. The beat was forceful. There was a long harsh systolic murmur heard best in the third intercostal space on both sides of the sternum. A roentgenogram of the chest confirmed that the heart was enlarged and showed exaggeration of the aortic arch. There was pulmonary congestion. On the day of his admission, the

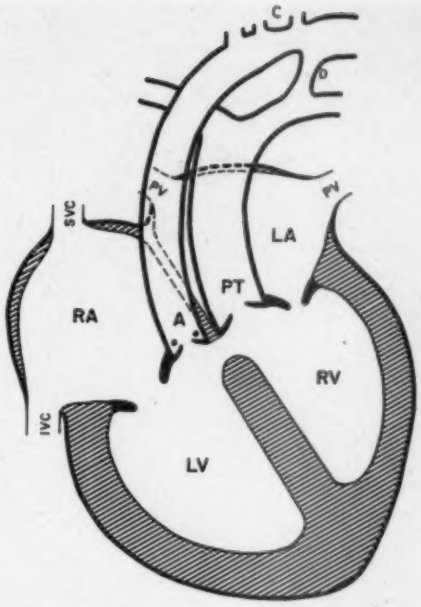

FIG. 22. Case 9. Diagrammatic sketch of heart. D = ductus arteriosus; other labels as in Figure 3.

child had an attack of cyanosis accompanied by marked lowering of the body temperature. He responded well to resuscitative measures at first but died suddenly in a similar attack on September 10, 1945.

Postmortem Examination: Aside from the findings in the heart, the pathologic diagnosis was: (1) marked passive congestion of the lungs and of the brain; (2) congenital defect of the right diaphragm; (3) congenital malformation of the kidneys; (4) double left ureter; (5) congenital absence of the gallbladder; (6) fatty degeneration of the liver.

Heart (Fig. 22). The heart was slightly enlarged. The apex was formed by the anterior ventricle. From the base two arterial trunks emerged, a larger situated to the left and a smaller situated to the right. The vessel on the left was identified as the pulmonary trunk. The anterior descending coronary artery emerged from between the two great vessels on the left, and followed a semicircular course from base to apex, the semicircle being convex to the right. The atrial appendage on the right lay anterior to the aorta. The atrial appendage on the left lay posterior to the pulmonary trunk. Only its tip could be seen on the anterior aspect of the heart.

The mutual relationships of the various chambers were as follows: the right atrium was in its usual position. It communicated with the morphologic left ventricle which lay anteriorly and to the left. The left atrium was in its usual position. It communicated with the morphologic right ventricle which lay posteriorly and to the right.

The right atrium was larger than the left atrium in this heart. It was larger than a normal right atrium of this age. Its wall was thicker than that of the left atrium in this heart and thicker than normal. It

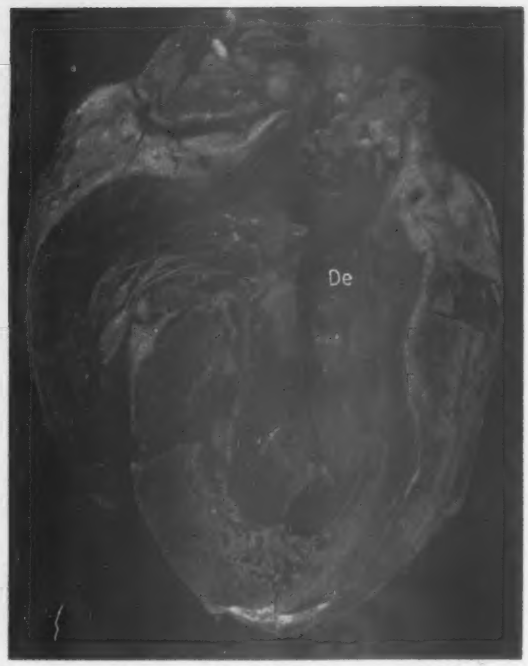

FIG. 23. Case 10. Septal view of morphologic left (right-sided) ventricle. A = aorta; P = pulmonary trunk.

received the superior and inferior venae cavae and coronary sinus in the usual manner. The eustachian and thebesian valves were normally formed. The limbus was well formed. There was a patency of the foramen ovale measuring 1 cm. in maximum dimension. The endocardium was diffusely thickened. The right atrium communicated with the morphologic left ventricle by way of an orifice which could not be identified as either tricuspid or mitral and will in consequence be called the right atrioventricular orifice. This orifice was larger than the opposite atrioventricular orifice in this heart. It was smaller than a normal tricuspid orifice but about normal in size for a mitral orifice in a child of this age. The right atrioventicular valve was composed of two indistinctly defined leaflets. Each leaflet was attached to an anterior and an inferior papillary muscle but the configuration of these leaflets was not characteristic of either A-V valve. It showed increased hemodynamic change as compared to the normal tricuspid valve, and slightly increased hemodynamic change as compared to the normal mitral valve of this age.

The morphologic left ventricle was larger than that of the opposite ventricle in this heart. It was larger than a normal left ventricle of this age. The wall was thicker than that of the opposite ventricle. It was thicker than the wall of either ventricle in a normal heart of this age. The endocardium appeared to be normal. There was a slit-like defect in the interventricular septum near the base measuring 1.5 cm. in length. The anterior septum was absent being replaced by an atypical band of crista musculature. The pars membranacea was absent, its site being included in the defect. The anterior wall of the defect consisted of a band of musculature, from which two ridges extended, one to the anterior wall of the morphologic left ventricle (accessory parietal band) and the other to the anterior wall of the morphologic right ventricle (parietal band). The defect entered the conus of the morphologic right ventricle. From the morphologic left ventricle emerged the aorta. Its orifice was smaller than that of the pulmonary orifice. It was smaller than either a normal pulmonary or aortic orifice of this age. The aortic valve was normally formed. It showed slightly increased hemodynamic change as compared to a normal aortic orifice of this age. The wall of the aorta was the same thickness as that of the pulmonary trunk. The brachiocephalic vessels were given off normally. There was a localized area of narrowing measuring 0.4 cm. in length between the origin of the left subclavian artery and the ductus arteriosus. The ductus arteriosus was widely patent. There was a left aortic arch. The descending aorta was normal in caliber.

The left atrium was smaller than the right atrium in this heart, but probably normal in size for this age. Its wall was thinner than that of the opposite atrium, but normal for this age. It received the four pulmonary veins in the usual manner. The endocardium was diffusely thickened throughout. This chamber communicated with the morphologic right ventricle by way of an orifice resembling a tricuspid orifice. This orifice was smaller than the opposite atrioventricular orifice in this heart, and smaller than either a normal mitral or tricuspid orifice of this age. The tricuspid valve was composed of three distinct leaflets. The anterior leaflet was attached to a small, short anterolateral papillary muscle to the septum. The medial leaflet was attached by chordae to the septum and to one short, small papillary muscle arising from the septum. The inferior leaflet was attached to three small inferior papillary muscles. This valve showed slightly increased hemodynamic change as compared to either a normal mitral or tricuspid valve of this age.

The morphologic right ventricle was smaller than the opposite ventricle in this heart. It was smaller than the normal right ventricle of this age. Its wall was thinner than that of the opposite ventricle. It was considerably thicker than that of a normal right ventricle and slightly thinner than that of a normal left ventricle. The endocardium of the sinus and conus was thickened. The parietal band of the crista was normal in position but was excavated. It was now seen that there was no anterior septum in this heart, but that the septal band of the crista separated the right outflow tract from the left outflow tract. This septal band was attached to two parietal bands as described above. Neither the aortic nor the pulmonic orifice was confluent with the defect. From the chamber of the morphologic right ventricle

emerged the pulmonary trunk. The pulmonary orifice was larger than the aortic orifice in this heart, and larger than a normal pulmonary or aortic orifice of this age. The pulmonary valve was normally formed. It showed increased hemodynamic change as compared to the normal pulmonic valve. The wall of the pulmonary trunk was the same thickness as that of the aorta. The pulmonary arteries were given off normally. The ductus arteriosus was widely patent leading directly into the descending aorta.

The right-sided coronary artery arose from the left anterior sinus of Valsalva. It gave off the anterior descending coronary artery, then continued as the right circumflex artery which gave off a branch to the anterior wall of the morphologic right ventricle. The left-sided coronary artery arose from the posterior sinus of Valsalva. It ran posterior to the pulmonary trunk to reach the atrioventricular sulcus where it became the left circumflex artery. This artery supplied the obtuse margin of the heart, gave off the posterior descending branch and continued in the atrioventricular sulcus to end as branches running to the acute margin of the heart. The anterior descending coronary veins joined branches from the acute margin of the heart and from the anterior aspect of the morphologic left ventricle to form a common vein which entered the right atrial appendage through a single small orifice. The posterior descending coronary veins joined veins from the posterior aspect of both ventricles, and from the anterior aspect of the morphologic right ventricle. It emptied into the coronary sinus in the usual way.

Anatomic Diagnosis:

I. Mixed levocardia (atria normal, ventricles inverted)
II. Complete transposition with fetal coarctation and ventricular septal defect complex
   A. Right atrial hypertrophy and dilatation
   B. Hypertrophy and dilatation of the morphologic left (right-sided) ventricle (hypertrophy and dilatation of the aortic ventricle)
   C. Hypertrophy of the morphologic right (left-sided) ventricle (hypertrophy of the pulmonic ventricle)
III. Widely patent ductus arteriosus

CASE 10. MIXED LEVOCARDIA WITH VENTRICULAR INVERSION, COMPLETE TRANSPOSITION WITH PULMONARY STENOSIS AND VENTRICULAR SEPTAL DEFECT

Clinical Summary: This twelve year old white girl was first seen at the Children's Memorial Hospital on July 29, 1957, with a history of tiring easily and of becoming breathless after mild or moderate exertion. Her mother stated that the child had become cyanosed soon after birth. At two and a half years of age, a diagnosis of transposition of the great vessels was made at another hospital. An artificial atrial septal defect was made surgically with improvement but not total removal of symptoms. Growth and development were slow and exercise tolerance was reduced. On examination, the child was seen to be thin, somewhat small and cyanosed. The point of maximum cardiac impulse was in the fifth intercostal space, just lateral to the nipple line. No thrills were palpable. A grade 2 to 3 blowing systolic murmur was present over the entire precordium, maximal at the apex. There was marked polycythemia (hemoglobin level 24.5 gm. per cent) with clubbing of the fingers and toes. An electrocardiogram showed complete A-V block, right heart strain, and possible right atrial hypertrophy. A modified Baffes procedure for transposition of the great vessels was performed on August 2, 1957. The right inferior pulmonary vein and the inferior vena cava were ligated, the inferior vena cava was anastomosed to the distal stump of the pulmonary vein by way of an aortic graft; the proximal stump was anastomosed to the wall of the right atrium. The child recovered from the anesthetic but died suddenly on the first postoperative day.

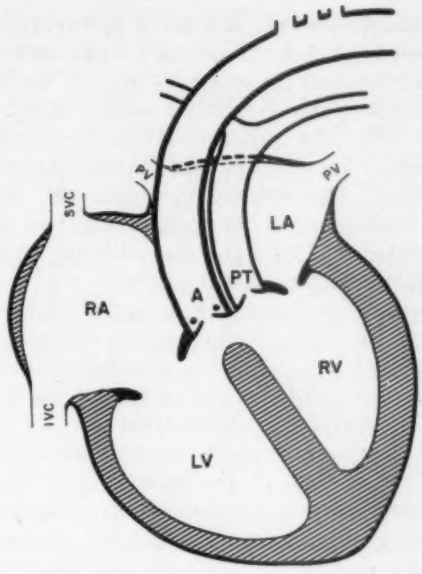

FIG. 24. Case 10. Diagrammatic sketch of heart. Labels as in Figure 3.

Postmortem Examination: Aside from the findings in the heart, the pathologic diagnosis was: (1) bilateral pulmonary congestion; (2) right hemothorax (minimal); (3) old pericardial adhesions.

Heart (Figs. 23, 24): The heart was enlarged. The apex was formed mainly by the ventricle on the right, but in part by the ventricle on the left. From the base two arterial trunks emerged, a larger situated anteriorly and to the right, and a smaller posteriorly and to the left. The larger was identified as the aorta. The anterior descending coronary artery emerged from between the pulmonary artery and aorta on the left, and ran in a more or less straight line over the anterior surface of the heart swinging to the left at the apex. The atrial appendage on the right lay to

the right of the aorta. The atrial appendage on the left nestled behind the pulmonary trunk and only its tip could be seen on the anterior surface of the heart.

The mutual relationships of the various chambers were as follows: the right atrium was in its normal position on the right. It communicated with the morphologic left ventricle, situtated on the right and anterior. The left atrium was in its usual position on the left. It communicated with the morphologic right ventricle, situated on the left and posterior.

The right atrium was larger than the left atrium in this heart. It was of about normal size for a right atrium of this age. Its wall was thicker than that of the opposite atrium in this heart and thicker than that of a normal right atrium of this age. It received the superior vena cava and coronary sinus in a normal manner. The entry of the inferior vena cava was normal before operation, according to the surgeon. According to the prosector, it had been transplanted as will be described. Likewise according to the prosector, the proximal stump of the right inferior pulmonary vein had been anastomosed to this chamber, as will be described. The eustachian valve was prominent. The thebesian valve was abnormally anchored to the inferior part of the eustachian valve. The limbus was well formed but described a wide arc. The septum primum was completely deficient in the region of the fossa ovalis producing a widely patent foramen ovale (secundum defect) measuring 2 cm. in greatest dimension. There was diffuse whitening and thickening of the endocardium of this chamber. The right atrium communicated with the morphologic left ventricle by way of an orifice resembling a mitral orifice. This orifice was larger than the opposite atrioventricular orifice in this heart. It was larger than a normal mitral orifice but of average size for a tricuspid orifice in a normal heart of this age. The valve was composed of two leaflets. The anterior leaflet was attached to an anterior group of papillary muscles and to a small group of thin inferior papillary muscles. The inferior leaflet was bifid; it was also attached to both the anterior and inferior group of papillary muscles. The posterior papillary muscles were attached to the parietal wall in a diffuse manner. This valve showed moderately increased hemodynamic change as compared to a normal tricuspid valve and slightly increased hemodynamic change as compared to a normal mitral valve.

The morphologic left ventricle was much larger than the opposite ventricle in this heart. It was of about normal size for a left ventricle of this age. Its wall was slightly thinner than that of the opposite ventricle in this heart, and thinner than that of a normal left ventricle, although it greatly exceeded that of a normal right ventricle of this age. The endocardium of this chamber was diffusely thickened. There was a defect in the ventricular septum at the base measuring 1.5 cm. in greatest dimension. It involved the pars membranacea and part of the anterior septum adjacent to it. The remainder of the anterior septum lay between the defect and the mouth of the aorta. The defect entered the morphologic right ventricle posterior to the crista supraventricularis and excavated the septal band. Neither the pulmonary nor aortic orifice was confluent with the mouth of the defect. From this chamber emerged the aorta. Because of the oblique position of the defect, the aorta straddled the ventricular septum, coming off about 25 per cent from the morphologic right ventricle. The aortic orifice was larger than the pulmonary orifice in this heart. It was of the same size as the normal aortic orifice. The aortic valve was composed of a left, and right anterior and posterior cusps. The left and right posterior cusps were markedly thickened. The right anterior cusp was thicker than normal, but it was less affected than the other two cusps. Thus this valve showed moderate to marked hemodynamic change as compared to a normal aortic valve at this age. The aorta was thicker than the pulmonary trunk, and the same size or slightly thicker than the normal aortic wall of this age. The brachiocephalic vessels were normal. There was a left aortic arch.

The left atrium was smaller than the right atrium in this heart. It was the same size or slightly smaller than a normal left atrium of this age. Its wall was thinner than that of the right atrium in this heart, but of average thickness for a normal left atrium. The entry of the left two and right upper pulmonary veins was normal. According to the prosector, the inferior vena cava had been surgically anastomosed to the distal stump of the divided right inferior pulmonary vein by way of an aortic graft, while the proximal stump had been anastomosed to the right atrium. The proximal two thirds of the endocardium was diffusely thickened. This chamber communicated with the morphologic right ventricle by way of an orifice identified as the tricuspid orifice. This orifice was smaller than the opposite orifice in this heart. It was smaller than a tricuspid orifice of this age, but of average size for a mitral orifice. The tricuspid valve was composed of an anterior and an incompletely divided inferomedial leaflet. The anterior leaflet was attached to two small anterolateral papillary muscles, and to the septum by way of a short, almost vestigial, papillary muscle. The inferomedial leaflet was attached by chordae to a group of small short papillary muscles arising from the septum and the inferior wall of the morphologic right ventricle. This valve showed increased hemodynamic change as compared to the normal mitral or tricuspid valve of this age.

The morphologic right ventricle was much smaller than the opposite ventricle in this heart and much smaller than a right ventricle of this age. Its wall was slightly thicker than that of the left ventricle in this heart. It was thicker than a normal right ventricle of this age, but thinner than a normal left ventricle. This chamber communicated with the opposite

ventricle by way of a ventricular septal defect previously described. The septal band of the crista supraventricularis was both excavated and divided into two parts by this defect. The parietal band was somewhat flattened. There was a separate subpulmonic conus. The wall of this conus was thinner than other parts of the right ventricle. Its inferior boundary was formed by a narrow ridge of thickened endocardium encircling the outflow tract just above the crista. In this conal chamber and immediately inferior to it, the endocardium was whitened and thickened. From this chamber emerged the pulmonary trunk. The pulmonary orifice was smaller than the aortic orifice in this heart, and somewhat smaller than a normal pulmonary orifice of this age. The pulmonary valve was normally formed. All three cusps were diffusely thickened. Thus this valve showed marked hemodynamic change as compared to a normal pulmonic valve of this age. The wall of the pulmonary trunk was thinner than that of the aorta. It was normal in thickness for this age. The main pulmonary arteries were given off normally. The ductus arteriosus was closed.

The right-sided coronary artery arose from the left sinus of Valsalva. It passed anterior to the aorta, giving off the anterior descending coronary artery; thereafter it formed the right circumflex artery. The left-sided coronary artery emerged from the right posterior sinus of Valsalva. It ran posterior to the pulmonary trunk to reach the left atrioventricular sulcus where it formed the left circumflex artery. This artery gave rise to branches which ran to the obtuse margin of the heart, and ended as the posterior descending coronary artery. The anterior descending vein joined branches from the anterior aspect of the morphologic left ventricle, and from the acute margin of the heart to form a common vein which drained into the right atrial appendage by way of one small and one large orifice. The posterior descending vein joined branches from the posterior aspect of both ventricles, and from part of the anterior aspect of the morphologic right ventricle. It emptied into the coronary sinus in the usual manner.

Anatomic Diagnosis:

I. Mixed levocardia (atria normal, ventricles inverted)
II. Complete transposition with pulmonary stenosis and ventricular septal defect
  A. Right atrial hypertrophy
  B. Atrophy of the morphologic left (right-sided) ventricle (normal aortic ventricle)
  C. Hypertrophy of the morphologic right (left-sided) ventricle (hypertrophy of the pulmonic ventricle)
  D. Infundibular pulmonic stenosis
  E. Ventricular septal defect
  F. Overriding aorta
III. Modified Baffes procedure
IV. Surgically altered atrial septal defect (secundum type)

CASE 11. MIXED LEVOCARDIA WITH ATRIAL INVERSION, COMPLETE TRANSPOSITION WITH PULMONARY STENOSIS AND VENTRICULAR SEPTAL DEFECT, ABNORMAL PULMONIC AND SYSTEMIC VENOUS RETURN

Clinical Summary: This nineteen year old white boy had suffered from shortness of breath, cyanosis and occasional attacks of sharp fleeting pains in the chest for as long as he could remember. He was first seen at the University of Illinois Research and Educational Hospitals in July, 1956, at the age of seventeen years. His symptoms had not increased in severity. There was clubbing of the fingers and some enlargement of the heart to the right of the midline. A thrill was felt over the right sternal margin associated with a grade 4 loud, harsh systolic murmur heard best over the second right interspace. This murmur was transmitted over the neck, the entire precordium, and to a lesser extent over the back. A chest roentgenogram showed decreased pulmonary vascularity, suggestive of pulmonary stenosis, a stomach bubble on the right and a right aortic arch. Right ventricular hypertrophy and delayed left ventricular conduction were seen on the electrocardiogram. He was admitted two years later for open heart surgery. A ventricular septal defect was closed without a graft, and an infundibular and valvular pulmonic stenosis was corrected under direct vision. Atrioventricular dissociation with a probable nodal rhythm developed after operation. He was discharged on the nineteenth postoperative day and appeared to be progressing well until his sudden death on the thirty-eight postoperative day, while attending the cardiac clinic.

Postmortem Examination: Aside from the findings in the heart, the pathologic diagnosis was: (1) inversion of the lungs, liver, spleen, stomach and intestines; (2) chronic passive hyperemia of the lungs, liver and spleen; (3) bilateral hemothorax; (4) old adhesive pericarditis; (5) subacute softening of the left cerebellar hemisphere.

Heart (*Figs. 25, 26, 27, 28*). The heart was enlarged and conical in shape. The apex was formed by the left ventricle. From the base two arterial trunks emerged, a larger situated anteriorly and to the right, and a smaller posteriorly and to the left. The anterior vessel was identified as the aorta. The anterior descending coronary artery emerged from between the two great vessels on the left, and proceeded downwards in a straight line from base to apex over the anterior aspect of the heart. The atrial appendage on the right was small and rested behind the aorta. The atrial appendage on the left was also small. It lay posterior to the aorta but anterior to the pulmonary trunk.

The mutual relationships of the various chambers were

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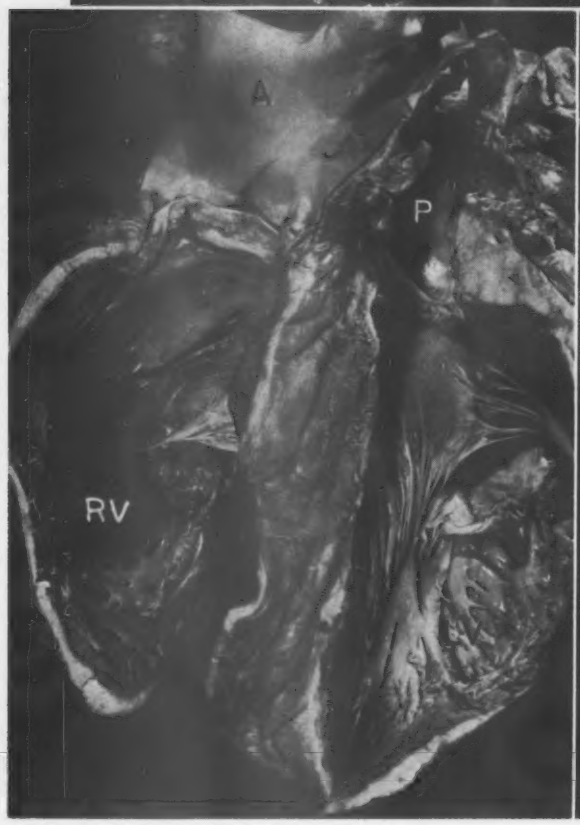

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FIG. 25. Case 11. Septal view of morphologic left (right-sided) atrium, tricuspid valve and inflow tract of right ventricle.

FIG. 26. Case 11. View from superior surface into outflow tracts of right and left ventricles. A = aorta; P = pulmonary trunk; RV = right ventricle.

FIG. 27. Case 11. View of outflow tract of left ventricle, showing two ventricular septal defects and pulmonary stenosis.

as follows: the morphologic left atrium lay anteriorly and to the right. It communicated with the right ventricle which was present in its normal position, anteriorly and to the right. The morphologic right atrium lay posteriorly and to the left. It communicated with the left ventricle which occupied its normal position, posteriorly and to the left.

The morphologic left atrium was smaller than the opposite atrium in this heart. It was larger than a normal left atrium and of about the same size as a normal right atrium of this age. Its wall was of about the same thickness as that of the opposite atrium in this heart. It was thicker than the wall of a normal left or right atrium of this age. It received the superior vena cava, the azygos vein and the two right pulmonary veins. The endocardium was normal

for this age. This chamber communicated with the right ventricle by way of an orifice identified as the tricuspid orifice. It was smaller than the mitral orifice in this heart, but of average size for a tricuspid orifice of this age. The tricuspid valve was abnormally formed. The anterior leaflet was attached to a small anterolateral papillary muscle, which arose exclusively from the anterior wall of the right ventricle. The medial part of this leaflet was attached to a papillary muscle arising from the septum. In addition, the conal aspect of this leaflet was connected to two further papillary muscles, a larger which proceeded to the parietal wall, and was the largest of all the papillary muscles in this ventricle, and a smaller which had the usual topography of the muscle of Lancisi. The medial and inferior leaflets were fused. The common leaflet so formed was attached to the septal papillary muscle, described above, to a small papillary muscle arising from the junction of the anterior and posterior walls, and to numerous chordae arising directly from the ventricular wall. This valve showed about the same degree of hemodynamic change as a normal tricuspid valve of this age, and much less than a normal mitral valve of this age.

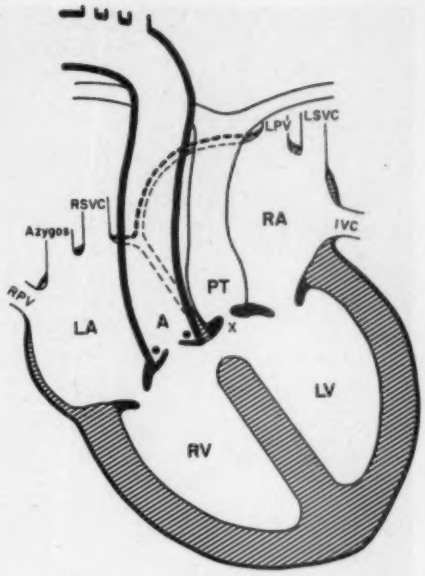

FIG. 28. Case 11. Diagrammatic sketch of heart. RPV = right pulmonary veins; LPV = left pulmonary veins; LSVC = left superior vena cava; RSVC = right superior vena cava; other labels as in Figure 3.

The right ventricle was the same size as that of the opposite ventricle in this heart. It was larger than a normal right ventricle of this age. Its wall was of the same thickness as that of the opposite ventricle in this heart, but much thicker than that of a normal right ventricle of this age. The crista supraventricularis was abnormally formed. The septal band was hypertrophied. The parietal band was flattened, and met the septal band to form a crista, which was excavated by the defect to be described. The endocardium of the outflow tract was markedly thickened and whitened. Mild diffuse thickening was also present throughout the inlet. From this chamber emerged the aorta. The aortic orifice was larger than the pulmonic orifice in this heart and larger than a normal aortic or pulmonic orifice of this age. The aortic valve was normally formed. This valve showed increased hemodynamic change as compared to either a normal aortic or pulmonic valve of this age. The coronary ostia were situated in the posterior sinuses of Valsalva. The wall of the aorta was thicker than that of the pulmonary trunk, and thicker than normal. There was a right aortic arch. The brachiocephalic vessels were given off in a mirror image position of the normal. The aorta descended to the right of the thoracic spine.

The morphologic right atrium was larger than the opposite atrium in this heart, and much larger than a normal right atrium of this age. Its wall was of about the same thickness as that of the opposite atrium in this heart, and thicker than that of a normal right or left atrium of this age. It received the inferior vena cava, a left superior vena cava, the coronary sinus and two pulmonary veins from the left lung. The eustachian valve was small. The thebesian valve was absent. The limbus was well formed. The foramen ovale was closed. The endocardium was diffusely thickened and whitened in excess of normal particularly over the septum, over the inferior wall, and around the mouths of the inferior vena cava and coronary sinus. This chamber communicated with the left ventricle by way of an orifice identified as the mitral orifice. It was larger than the tricuspid orifice in this heart, and much larger than a normal mitral orifice of this age. The mitral valve was normally formed. The anterior and inferior papillary muscles were normal. This valve showed increased hemodynamic change as compared to a normal mitral or tricuspid valve.

The left ventricle was the same size as the opposite ventricle in this heart. It was larger than normal for this age. Its wall was of the same thickness as that of the opposite ventricle, but thinner than that of a normal left ventricle of this age. There was a defect in the ventricular septum at its base, measuring about 1.2 cm. in greatest dimension. Numerous sutures were visible in the inferior portion of this defect. The defect involved the region of the pars membranacea, and part of the anterior septum adjacent to it. It was confluent with the mouth of the pulmonary trunk. It entered the lower part of the conus of the right ventricle slightly excavating the crista supraventricularis. In addition there was a separate, pin hole defect measuring about 0.1 cm. in diameter in the septum adjacent and posterior to the larger defect. This smaller defect entered the sinus of the right ventricle just posterior to the entrance of the larger defect. The endocardium of the septal surface of the left ventricle was markedly thickened and whitened, in particular in the region of the defects

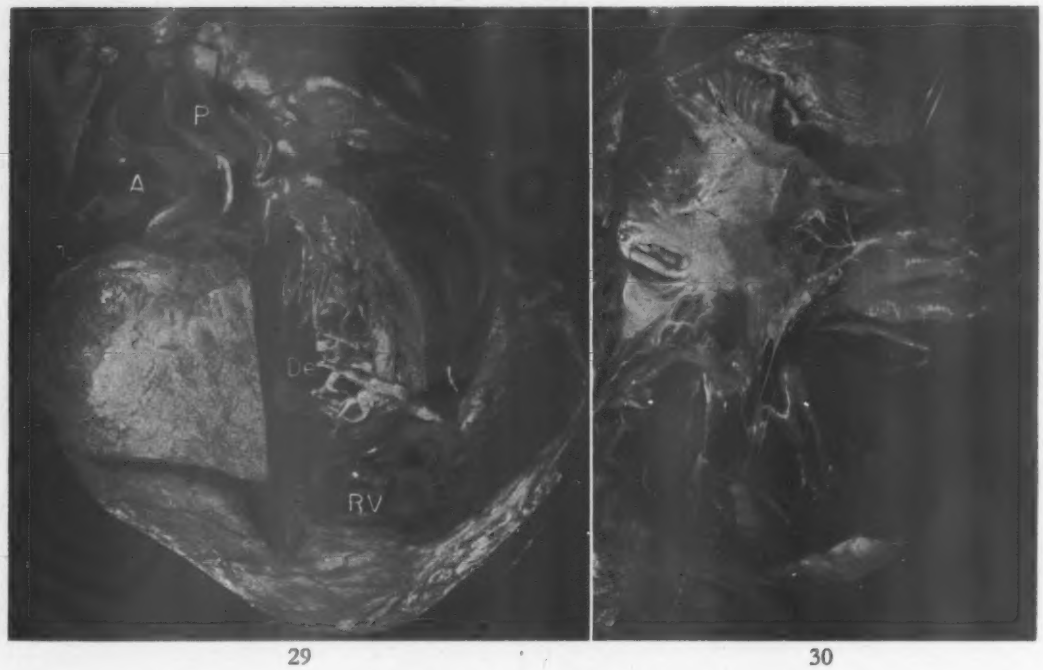

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FIG. 29. Case 12. View of septal surface of right ventricle. A = aorta; P = pulmonary trunk; De = ventricular septal defect; RV = right ventricle.

FIG. 30. Case 12. View of right atrium, mitral valve and inflow tract of left ventricle.

described above. From this chamber emerged the pulmonary trunk. The pulmonic orifice was much smaller than that of the aortic orifice in this heart, and smaller than normal for this age. The pulmonic valve was normally formed. The cusps were thickened in a more or less even manner throughout. All three sinuses of Valsalva were shallow. The wall of the pulmonic trunk was thinner than that of the aorta in this heart, and probably slightly thinner than normal for this age. The main pulmonary arteries arose normally. The ductus arteriosus was closed.

The right-sided main coronary artery arose from the right posterior sinus of Valsalva. It gave rise to the right circumflex branch, which, in turn gave rise to the posterior descending coronary artery. The left-sided coronary artery arose from the left posterior sinus of Valsalva. It gave rise to the anterior descending branch and to the left circumflex coronary artery. The anterior descending vein joined veins from the anterior aspect of the left ventricle, and from the obtuse margin of the heart, to form a common vein which opened by a single orifice into the morphologic right atrial appendage. The posterior descending vein entered the morphologic right atrium by way of a small orifice lying inferior to the opening of the main coronary sinus. The coronary sinus ran in the atrioventricular sulcus in the opposite direction to normal. It received branches from the anterior aspect and the acute margin of the heart.

Anatomic Diagnosis:

I. Mixed levocardia (atria inverted, ventricles normal)
II. Complete transposition of the arterial trunks with pulmonary stenosis and ventricular septal defect
   A. Hypertrophy of the morphologic left atrium
   B. Hypertrophy and dilatation of the right ventricle
   C. Hypertrophy and dilatation of the morphologic right atrium
   D. Dilatation of the left ventricle
   E. Pulmonic valvular stenosis
   F. Post-stenotic dilatation of the pulmonic trunk
   G. Dilatation of the aorta
III. Abnormal pulmonic and systemic venous return
   A. Persistent left superior vena cava
   B. Drainage of the right pulmonary veins, right superior vena cava and azygos vein into the morphologic left atrium
   C. Drainage of the left pulmonary veins, left superior vena cava, inferior vena cava and coronary sinus into the morphologic right atrium
IV. Right aortic arch
V. Surgical intervention (closure of ventricular septal defect)

CASE 12. MIXED LEVOCARDIA, ATYPICAL, TAUSSIG-BING COMPLEX WITH EBSTEIN'S COMPLEX

Clinical Summary: This eight year old white girl was known to have had a cardiac murmur since the

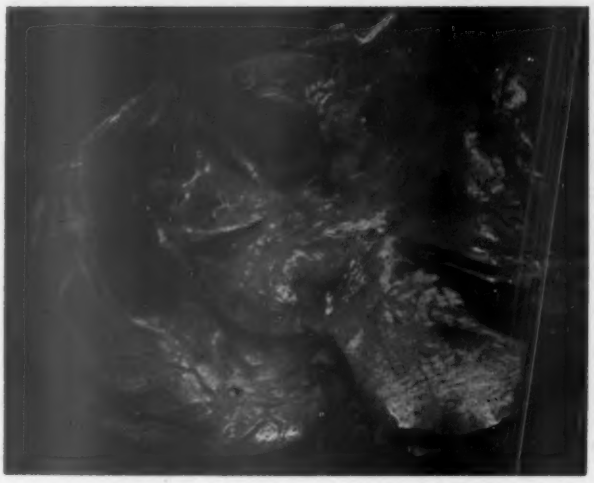

FIG. 31. Case 12. View of left atrium, tricuspid valve and inflow tract of right ventricle.

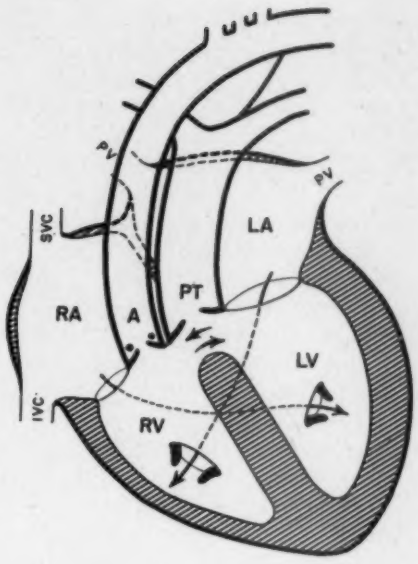

FIG. 32. Case 12. Diagrammatic sketch of heart. Labels as in Figure 3.

age of two weeks. She was admitted to the Children's Memorial Hospital for the first time in May, 1956, at the age of six years. On examination, she was fairly well nourished and acyanotic at rest. The heart was enlarged. There was a coarse precordial thrill and harsh grade 4 systolic murmur, maximal at the fourth left intercostal space and an apical mid-diastolic murmur. An electrocardiogram showed marked left heart strain. Cardiac catheterization demonstrated a bidirectional shunt, probably at the ventricular level, with severe pulmonary hypertension. She was readmitted on July 7, 1958 in acute respiratory distress with a history of having had a cold three weeks earlier. She was markedly cyanotic and was in congestive heart failure. Therapy was of no avail and the child died within a few hours of admission.

Postmortem Examination: Aside from the findings in the heart, the pathologic diagnosis was: (1) chronic passive congestion of liver, kidneys, and spleen; (2) hydropericardium; (3) bilateral hydrothorax; (4) ascites; (5) bilateral bronchopneumonia with infarction of the right and left lower lobes.

Heart (*Figs. 29, 30, 31, 32*). The heart was enlarged. The base-apex axis pointed toward the left. From the right side of the base, two arterial trunks emerged, a smaller situated anteriorly and to the right, and a larger situated posteriorly and to the left. The anterior vessel was identified as the aorta. The anterior descending coronary artery was in its usual position. It arose from the left-sided main coronary artery about 1 to 1.5 cm. beyond its origin from the left lateral margin of the aorta.

The mutual relationships of the various chambers were very disturbed. The morphologic right atrium was situated anteriorly, to the right and caudally, while the morphologic left atrium was situated posteriorly, to the left and cranially. Thus the large atrial appendage seen externally belonged to the left atrium, and the smaller one belonged to the right atrium. The left atrium communicated with the morphologic right ventricle which was situated anteriorly and to the right, and the right atrium communicated with the morphologic left ventricle, which was situated posteriorly and to the left. The apex was formed by the morphologic left ventricle. Thus it became clear that the atria and ventricles were situated almost in their correct positions, even though they communicated abnormally.

The right atrium was smaller than the left atrium in this heart, but slightly larger than a normal right atrium of this age. Its wall was of about the same thickness as that of the left atrium, and thicker than that of a normal right atrium of this age. It received the superior and inferior venae cavae and coronary sinus in a normal manner. The eustachian valve was markedly enlarged, and was connected by numerous strands to various points around the coronary sinus. Some of these strands might have been considered to be part of the thebesian valve. The opening at the coronary sinus was moderately large. The endocardial lining of this chamber was diffusely whitened and thickened, particularly over the septal surface. The limbus was well formed. There was a patent foramen ovale measuring about 1 cm. in greatest dimension. The right atrium was connected with the morphologic left ventricle by way of an orifice guarded by a mitral valve. This orifice was smaller than the tricuspid orifice in this heart, but larger than the mitral or tricuspid orifice in a normal heart of this age. The valve and valvular apparatus was normally formed, but the anterior and posterior groups of papillary muscles had a broader attachment than normal, and their component parts were more discreet. As compared to the normal mitral valve it showed slightly increased hemodynamic change; as compared with a normal tricuspid valve it showed marked hemodynamic change.

The morphologic left ventricle was slightly larger than the opposite ventricle in this heart, and larger than a normal left ventricle of this age. Its wall was thicker than that of the opposite ventricle. It was about the same thickness as a normal left ventricle, but thicker than a normal right ventricle of this age. The endocardial lining was normal. In the angle between the anterior papillary muscle and the septum there was a powerful ridge which proceeded from the base to the anterior wall of this chamber. The ventricular septum on the left presented an abnormal architecture in its apical region. There were several large bands of muscle instead of the fine trabeculae usually seen. In addition, there were two powerful bands on the septum close to the anterior wall, and adjacent to the large band previously described. The ventricular septum at its base presented a large defect measuring about 2.5 cm. in greatest dimension. This defect was covered in part by the tricuspid valve (left atrioventricular valve). It entered the right ventricle beneath the crista, at the junction of the upper part of the sinus and the lower part of the conus. The pulmonary trunk overrode the septum, to emerge slightly from the left ventricle.

The left atrium was larger than the right atrium in this heart, and much larger than normal for this age. Its wall was of about the same thickness as that of the right atrium but thicker than that of a normal left atrium of this age. This chamber received the four pulmonary veins in a normal manner. The endocardial lining was whitened and thickened. It was markedly geographic over the septal surface and over the inferior wall of the atrium. It was connected to the morphologic right ventricle by way of an orifice guarded by a tricuspid valve. This orifice was larger than the mitral orifice in this heart, and much larger than a normal tricuspid or mitral orifice of this age. The tricuspid (left atrioventricular) valve was markedly abnormal. There appeared to be an inferior, a large anterior and a medial leaflet. The inferior leaflet was connected to an inferior papillary muscle. The anterior leaflet was very large and connected by numerous irregular chordae to the anterior wall of the right ventricle and to the margin of the defect. Some of these chordae were very thick. The medial leaflet was connected by irregular chordae to the septum. The base of the inferior leaflet was pushed downward into the right ventricle for a distance of about 1.5 cm. Thus there were considerable adhesions of parts of the medial leaflet to the right ventricular septal wall. The effect of these adhesions was to produce an area of nonfunctioning valve tissue measuring 1 cm. The endocardium proximal to this region in the ventricle and adjacent atrium was tremendously thickened. As compared to a normal tricuspid or mitral valve, this valve presented marked diffuse hemodynamic change.

The morphologic right ventricle was slightly smaller than the opposite ventricle in this heart. It was of about average size for a right ventricle of this age. Its wall was thinner than that of the opposite ventricle. It was much thicker than that of a normal right ventricle, but thinner than a normal left ventricle of this age. The endocardium was diffusely thickened and whitened, particularly over the wall of the outflow tract, in the region of the crista supraventricularis and around the septal defect. This ventricle was remarkable in that its inlet lay on a more cranial level than its outlet. As a matter of fact, the position of the inlet was precisely in the spot where one would expect the outlet to be. The crista supraventricularis was abnormally formed. What appeared to be the septal band of the crista proceeded to the base and became continuous with a powerful ridge which lay at the root of the aorta. One part of this ridge formed part of the border of the defect, as did the septal band itself. The architecture of the muscle bundles was somewhat reminiscent of the Taussig-Bing heart. From this chamber emerged both the aorta and pulmonary trunk. The pulmonary trunk straddled the ventricular septum coming off from both sides. The pulmonic orifice was larger than the aortic orifice in this heart, and was very slightly larger than normal. Its valve was normally formed. As compared to the normal pulmonic or aortic valve, it presented marked hemodynamic change. The wall of the pulmonary trunk appeared to be of the same thickness as that of the aorta, and of normal thickness for this age. It gave off the two pulmonary branches in a normal manner. The ductus arteriosus was closed. From the right ventricle also emerged the aorta. As pointed out previously, the aortic orifice was removed from the defect and guarded from it by the powerful muscular ridge previously described. The aortic orifice was smaller than that of the pulmonary trunk. Its valve was normally formed. As compared to the normal aortic valve it presented no increased hemodynamic change. As compared to a normal pulmonic valve it presented possible or questionable hemodynamic change. The ascending aorta was smaller than the pulmonary trunk. Its wall was of about the same thickness as that of the pulmonic trunk, and thinner than normal. There was a left aortic arch. The brachiocephalic vessels were given off normally. There was a mild contraction band in the aorta in the region of the ligamentum arteriosum. This was insufficient to call frank coarctation. Distal to this point, the aorta was wider than proximal to it.

The right-sided coronary artery emerged from the right posterior sinus of Valsalva. It gave off a branch running to the acute margin of the heart, and continued in the atrioventricular sulcus as the right circumflex artery to reach the posterior aspect of the heart. It gave off the posterior descending coronary artery. The left-sided coronary artery emerged from the left posterior sinus of Valsalva.

Immediately after its origin it gave off a cristal branch. It then continued for 1 cm. after which it supplied the anterior descending coronary artery. It continued as the left circumflex artery running in the atrioventricular sulcus. This gave off the obtuse marginal branch and several other small twigs to the posterolateral portion of the morphologic left ventricle. The coronary venous drainage was normal.

Anatomic Diagnosis:

I. Mixed levocardia (atria and ventricles in relatively normal position)
II. Anatomic Taussig-Bing complex with Ebstein's complex. Physiologic ventricular septal defect with overriding pulmonary artery and Ebstein's complex of "left" A-V valve
   A. Right atrial hypertrophy and dilatation
   B. Dilatation and hypertrophy of the morphologic left ventricle (hypertrophy of the pulmonic ventricle)
   C. Left atrial hypertrophy and dilatation
   D. Hypertrophy of the morphologic right ventricle
   E. Overriding and dilated pulmonary trunk
   F. Ventricular septal defect
   G. Hypoplasia of the aorta
   H. Patent foramen ovale
   I. Abnormal eustachian valve

CASE 13. MIXED LEVOCARDIA, ATYPICAL, PARTIAL TRANSPOSITION WITH PULMONARY STENOSIS, VENTRICULAR SEPTAL DEFECT AND ABNORMAL VENOUS DRAINAGE

Clinical Summary: This five week old male infant was born on May 3, 1958 after an uncomplicated pregnancy lasting thirty-six weeks. He weighed 5 pounds, 8 ounces at birth, and for the first two days of life appeared healthy. Thereafter he began to vomit repeatedly, and failed to pass stools. On May 7, 1958 a laparotomy was performed, revealing inversion of the spleen, liver and stomach, and multiple atretic areas in the small intestine. Three operations were performed to relieve this condition. By June 1 the baby began to pass stools. In addition, a congenital heart lesion had been suspected and on June 5, 1958 he was transferred to the University of Illinois Research and Educational Hospitals. On admission, the pulse was 130 per minute. There was no bulging of the precordium and no parasternal lift. There was a grade 2 palpable thrill at the third to fourth left intercostal space. S_1 was maximal at the fourth left interspace and S_2 was maximal at the third left interspace. There were no abnormal findings in the lungs and no clinical evidence of heart failure. The baby became cyanosed on crying, and eventually was continuously cyanotic. The pulse became irregular and the respirations periodic. He died June 8, 1958.

Postmortem Examination: Aside from the findings in the heart, the pathologic diagnosis was: (1) inversion of the liver, stomach and spleen; (2) atresia of the small bowel (treated by three laparotomies) with resection and anastomoses, and residual partial small intestinal obstruction; (3) malrotation of the colon; (4) bilobed spleen; (5) marked chronic passive hyperemia of the liver; (6) infarcts of the liver.

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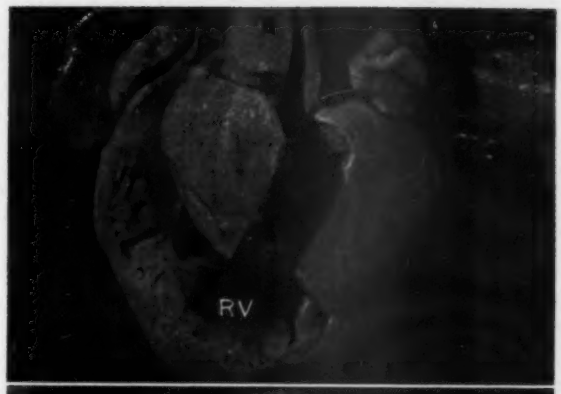

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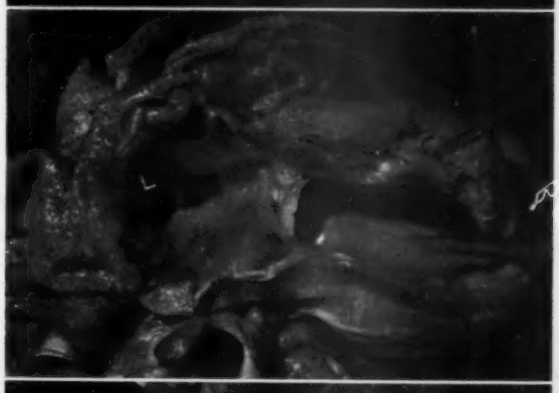

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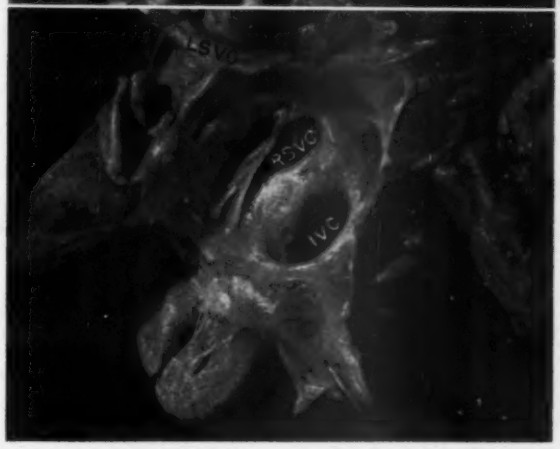

FIG. 33. Case 13. Combined external and septal view of right ventricle and efferent vessels. A = aorta; P = pulmonary trunk; RV = right ventricle.

FIG. 34. Case 13. View of right atrium, mitral valve and inflow tract of left ventricle. L = limbus fossa ovalis.

FIG. 35. Case 13. View of left atrium, tricuspid valve and inflow tract of right ventricle. LSVC = left superior vena cava; RSVC = right superior vena cava; IVC = inferior vena cava; LPV = left pulmonary vein.

Heart (*Figs. 33, 34, 35, 36*). The heart was slightly enlarged. It was bizarre in shape. The

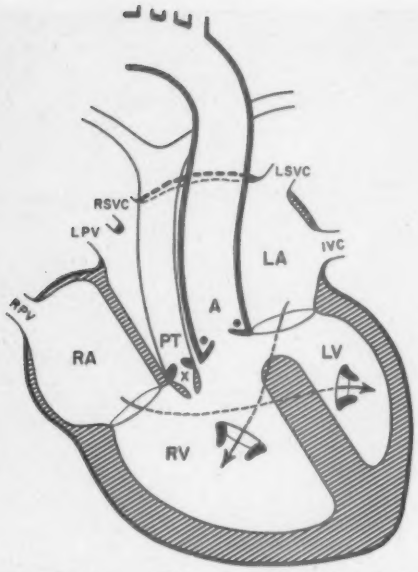

FIG. 36. Case 13. Diagrammatic sketch of heart. LPV = left pulmonary veins; RPV = right pulmonary veins; RSVC = right superior vena cava; LSVC = left superior vena cava; X = infundibular and valvular stenosis.

apex was formed by the posterior ventricle. There was a prominent hump at the base of the anterior afferent vessel. From the right side of the base two vessels emerged, a larger situated anteriorly and to the left, and a smaller situated posteriorly and to the right. The anterior vessel was identified as the aorta. The anterior descending coronary artery was in its usual position, but was seen to arise from a main left artery which ran horizontally from the aorta. The atrial appendage on the right lay to the right of the pulmonic trunk. The atrial appendage on the left lay to the left and posterior to the aortic trunk and was well visualized.

The mutual relationships of the various chambers was as follows: the right atrium was situated anteriorly, to the right and caudally. This communicated with the morphologic left ventricle which lay posteriorly, to the left and slightly caudally. The left atrium was situated posteriorly, to the left and cranially. It communicated with the morphologic right ventricle which lay anteriorly, to the right and slightly cranially.

The right atrium was much smaller than the opposite atrium in this heart, and much smaller than a normal right atrium. Its wall was the same size as that of the opposite atrium and probably thicker than normal for this age. It received the two right pulmonary veins. The endocardium of this chamber was either normal or slightly thinner than normal for this age. The limbus was well formed. The septum primum was markedly defective in the region of the fossa producing a patency measuring 0.8 cm. in maximum dimension. The right atrium communicated with the morphologic left ventricle by way of an orifice, considered to be the mitral orifice. This orifice was smaller than the opposite atrioventricular orifice in this heart, and smaller than a mitral or tricuspid orifice in an infant of this age. It was guarded by a typical mitral valve. The anterior and inferior leaflets were normally formed and were attached to an anterior and an inferior group of papillary muscles in the usual way. As compared to the normal mitral valve, this valve showed less hemodynamic change than normal for this age. As compared to the normal tricuspid valve of this age, it appeared to show the normal amount of hemodynamic change.

The morphologic left ventricle was smaller than the opposite ventricle in this heart, and smaller than a normal left ventricle of this age. Its wall was thinner than that of the opposite ventricle. It was somewhat thinner than normal for a normal left ventricle, but normal for a right ventricle of this age. The endocardial lining of this chamber was normal. The only outlet of this chamber was a defect in the septum measuring 0.6 cm. in maximum dimension. This defect involved the anterior septum and the pars membranacea but was not confluent with the mouth of either efferent vessel. It entered the lower part of the conus of the morphologic right ventricle adjacent to the anterior leaflet of the tricuspid valve.

The left atrium was dilated, being larger than the opposite atrium, and larger than a normal left atrium of this age. Its wall was the same thickness as that of the opposite atrium and was probably normal for this age. It received the pulmonary veins from the left lung, the coronary sinus, the inferior vena cava, and a right and left superior vena cava. There was no eustachian or thebesian valve. The endocardial lining was normal. This chamber communicated with the morphologic right ventricle by way of an orifice which was considered to be the tricuspid orifice. It was larger than the opposite atrioventricular orifice in this heart. It was smaller than a normal tricuspid orifice of this age, and the same size or slightly smaller than a normal mitral orifice. It was guarded by a typical tricuspid valve. The anterior leaflet was normal in shape. It was attached to two distinct anterior papillary muscles. The medial and inferior leaflets were normal. As compared to the normal tricuspid or mitral valve of this age, it showed the usual hemodynamic change.

The morphologic right ventricle was larger than the left ventricle and larger than a normal right ventricle of this age. Its wall was thicker than that of the left ventricle in this heart, and thicker than either a normal left or right ventricle. The crista supraventricularis was altered by the ventricular septum described above. The septal band was formed by two portions, which forked at the base, the anterior fork being continuous with one part of the parietal band, thus forming the crista. Another parietal band lay adjacent to the anterior leaflet of the tricuspid valve. The infundibular portion of the

pulmonic outflow tract was narrowed. The endocardial lining of this area was slightly thickened and whitened. The pulmonic orifice was smaller than the aortic orifice, and smaller than normal. It was guarded by a bicuspid valve, which showed no remarkable change. The pulmonary trunk was narrow. Its wall was thinner than that of the aorta, and thinner than normal. It gave rise to the two main pulmonary arteries in the usual manner. The ductus arteriosus was closed. The aortic orifice was much larger than the pulmonic orifice in this heart, and larger than a normal aortic orifice of this age. The aortic valve was normally formed. As compared to a normal aortic valve it showed the usual hemodynamic change. As compared to a normal pulmonic valve it showed increased hemodynamic change. The wall of the aorta was thicker than that of the pulmonary trunk, but of normal thickness for this age. There was a right aortic arch. The brachiocephalic vessels were given off in mirror-image of the normal. The descending aorta lay to the right of the vertebral column.

The right-sided coronary artery emerged from the right posterior sinus of Valsalva. It formed the right circumflex and posterior descending coronary arteries. The left-sided coronary artery emerged from the left posterior sinus of Valsalva. It gave off the left circumflex which travelled horizontally, eventually giving off the anterior descending coronary artery. The anterior descending vein and veins from the left margin of the heart drained into the coronary veins which opened into the left atrium. The posterior vein and veins from the right lateral margin of the heart drained into the left atrium by way of a small orifice situated superior to the mouth of the coronary sinus.

Anatomic Diagnosis:

I. Mixed levocardia (atria and ventricles in relatively normal position)
II. Partial, inverted, transposition with pulmonary stenosis complex
  A. Double outlet right ventricle
  B. Ventricular septal defect
  C. Infundibular and pulmonary valvular stenosis
  D. Biscuspid pulmonic valve
  E. Hypertrophy and dilatation of the right ventricle
  F. Atrophy of the left ventricle
III. Abnormal venous drainage
  A. Entry of the right pulmonary veins into the right atrium
  B. Entry of the left pulmonary veins, right superior and inferior vena cava and coronary sinus into the left atrium
  C. Persistent left superior vena cava draining into the left atrium
  D. Hypertrophy and dilatation of the left atrium
  E. Atrophy of the right atrium

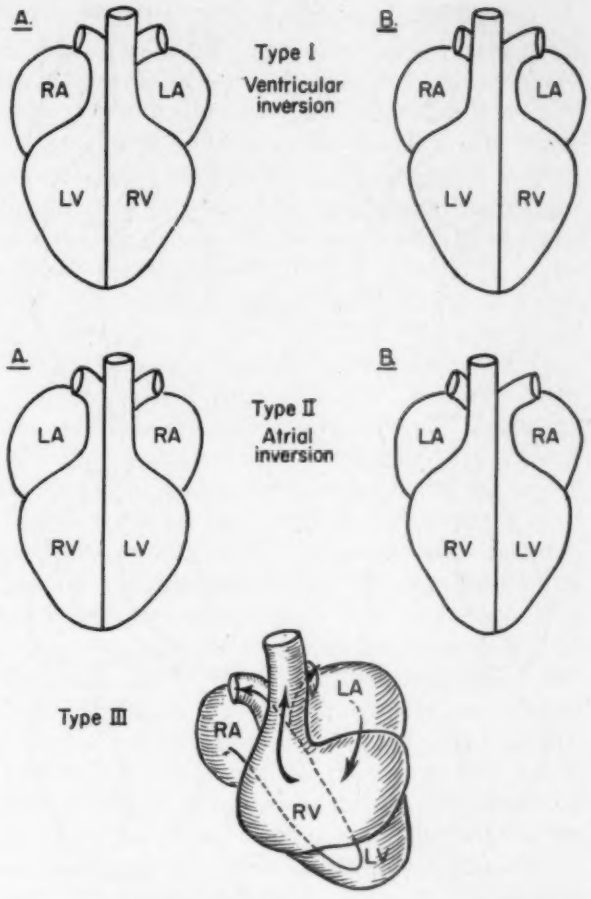

FIG. 37. Types of mixed levocardia: IA = with ventricular inversion and complete, inverted transposition of arterial trunks. IB = with ventricular inversion and complete, noninverted transposition of arterial trunks. IIA = with atrial inversion with normal position of efferent vessels. IIB = with atrial inversion and complete transposition of arterial trunks. III = atria and ventricles in relatively normal positions but abnormally connected.

IV. Atrial septal defect (secundum type)
V. Absent eustachian and thebesian valves
VI. Right aortic arch

COMMENT

There are three types of mixed levocardia in our material (Fig. 37): type I—atria normal, ventricles inverted; type II—ventricles normal, atria inverted; and type III—atria and ventricles in somewhat normal position, but abnormally connected. Type I presents two subtypes: (A) with inverted transposition and (B) with complete transposition (noninverted).

Type IA (mixed levocardia: atria normal, ventricles inverted; with complete inverted transposition): In this type, the pulmonary artery emerges from the morphologic left (right-sided) ventricle and the aorta from the morphologic

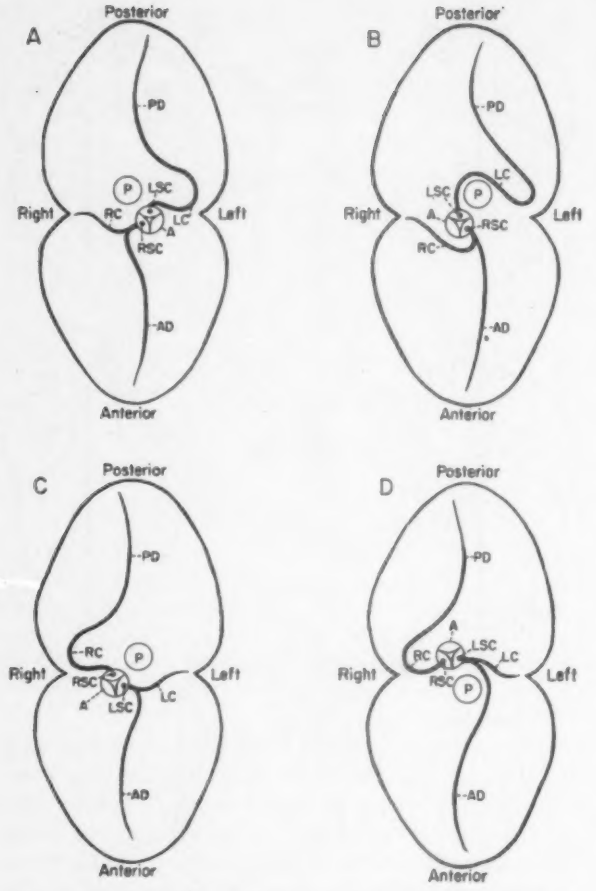

FIG. 38. Schematized coronary arterial origin and distribution in (A) mixed levocardia (type IA); (B) mixed levocardia (type IB); (C) pure levocardia with complete transposition of arterial trunks; (D) normal. Posterior and anterior walls and right and left A-V sulcuses are roughly indicated. After Liebow and MacFarland.[18] A = aorta; P = pulmonary artery; RSC = right-sided coronary sinus; LSC = left-sided coronary sinus; LC = left circumflex; AD = anterior descending; RC = right circumflex; PD = posterior descending.

right (left-sided) ventricle with the arterial trunk ostia in mirror image of complete transposition. The correct circulation is often reestablished and hence the term "corrected" may be used in some cases. This type of heart has certain characteristics regardless of the pathologic complex present. Some of these characteristics are gleaned from our material. However, a complete statement of the characteristics of the heart with this type of inverted transposition, and no other anomaly, cannot be made from our material because all our specimens are associated with pathologic complexes.

The external morphology of this type of heart is as follows: the aorta emerges anteriorly and to the left (with respect to the anterior aspect of the heart), and the pulmonary artery posteriorly and to the right (Figs. 1, 9, 19). The left border of the heart is often sharply rounded, so that the radius of the upper part of the curved segment is almost at right angles to the radius of the apical part (Fig. 9). The anterior surface of the heart may look like the normal posterior surface (Figs. 1, 19). The left atrial appendage is barely seen, or not seen at all on the anterior aspect of the heart. The right-sided coronary artery emerges from the right anterior sinus of Valsalva, between the aorta and pulmonary artery on their right aspect, and gives off the anterior descending and the right circumflex arteries (Fig. 38). The anterior descending branch proceeds toward the apex lying in the midregion of the anterior surface. The left-sided coronary artery emerges from the posterior sinus of Valsalva and forms the left circumflex artery and, usually, the posterior descending artery. Occasionally, the left-sided coronary artery is hypoplastic and the right-sided vessel forms the posterior descending artery. Large subepicardial veins drain the posterior surfaces and the obtuse margin of the heart and empty into the coronary sinus (Fig. 39). The anterior descending vein and veins from the acute margin of the heart open into the right atrial appendage by way of one or more small unguarded ostia.

Internally, the A-V valves correspond to the distal chamber. The right A-V (mitral) valve is more delicate than the normal mitral valve, provided that there is no superimposed hemodynamic force related to pathologic complexes. The corresponding anterior and posterior papillary muscle groups often have a wider attachment to the walls (Fig. 12), and the component muscles are smaller than normal in the absence of pathologic complexes. The left A-V (tricuspid) valve is much more abnormal than the mitral valve. The exact delineation into three leaflets may not be apparent. The leaflets are markedly thickened as compared to the normal tricuspid valve (Fig. 2). The papillary muscles are usually markedly abnormal (Figs. 5, 7, 10) and at times bizarre (Fig. 10); therefore, the tendency for left A-V valve insufficiency (Fig. 2), stenosis (Fig. 17), or Ebstein's (Fig. 7) and associated malformations of the inlet of the morphologic right (left-sided) ventricle (Figs. 10, 17). The morphologic left (right-sided) ventricle in the absence of pathologic complexes is thinner than the normal left ventricle. It is common to find a muscle band or bands extending from the base of the septum toward the

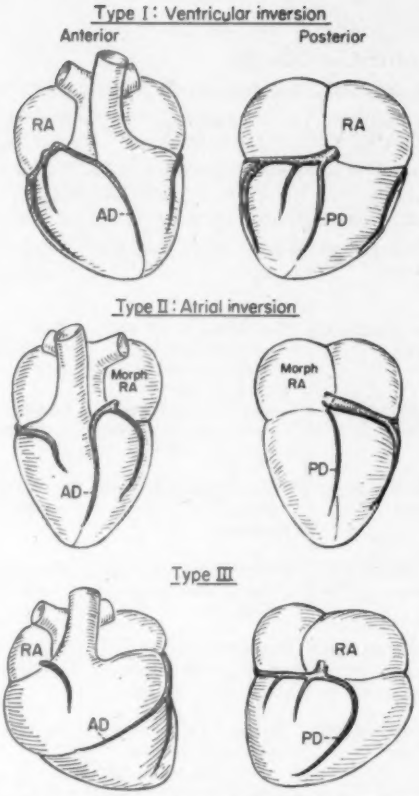

FIG. 39. Schematized diagrams of the coronary venous circulation in mixed levocardia. RA = right atrium; AD = anterior descending vein; PD = posterior descending vein.

apex, in the angle between the septum and the inferior wall, adjacent to the A-V valve (Figs. 12, 14 and 16). The pars membranacea is abnormally large in many cases, especially in the atrioventricular portion. It is apparent, as pointed out by Walmsley,[14] that the atrioventricular septum communicates between the left atrium and the morphologic left (right-sided) ventricle. The morphologic right (left-sided) ventricle is thicker than the normal right ventricle. The septal and parietal bands of the crista are markedly hypertrophied (Fig. 20). The septal band often presents offshoots at right angles to it, passing to the anterior wall-septal angle. The parietal band is characteristically flattened (Fig. 20). The crista sometimes is thinner than normal. The hemodynamic changes in the aortic and pulmonic valves and in the endocardium of all chambers in mixed levocardia with inverted transposition without anomalies cannot be accurately evaluated in our cases because of the accompanying congenital or acquired pathologic complexes.

The various complexes associated with the eight cases in type IA and other characteristics of these cases are presented in Table IV.

1. Left A-V valve insufficiency (*Case 1, Figs. 1, 2, 3*). The basic feature of this complex is the abnormally formed and hemodynamically altered left A-V (tricuspid) valve with insufficiency and its hemodynamic effects on the myocardium and endocardium. An added feature in our case was the entry of the coronary sinus into the left atrium which negates the term "corrected" transposition.

2. Ventricular septal defect and abnormal left A-V valve (*Case 5, Figs. 12, 13*). The ventricular septal defect was situated at the base of the ventricular septum but was not confluent with the mouth of the pulmonary artery. It entered the morphologic right (left-sided) ventricle in the lower part of the conus and in the upper part of the sinus and impinged upon the tricuspid valve. The latter was abnormally formed, but no insufficiency could be ascertained by pathologic examination. The complex was typical of ventricular septal defect with left to right shunt and pulmonary hypertension.

3. Ventricular septal defect with pulmonic stenosis and abnormal left A-V valve (*Case 6, Figs. 14, 15*). The defect was similar to the defect in Case 5. The pulmonic stenosis was mild. The complex is typical of that of left to right shunt at the ventricular level with mild pulmonic stenosis.

4. Ventricular septal defect and left A-V valvular stenosis (*Case 4, Figs. 9, 10, 11*). The defect was present in its usual position. The left A-V valve, however, now showed marked abnormality coupled with an abnormal architecture of the inflow tract of the morphologic right (left-sided) ventricle. The physiologic results of these appeared to have been mild stenosis of the left A-V orifice. Thus, this complex is typical of left to right shunt at the ventricular level with mild left A-V valve (tricuspid) stenosis.

5. Ventricular septal defect, pulmonic stenosis, overriding aorta and left A-V valvular stenosis (*Case 7, Figs. 16, 17, 18*). In this type, the ventricular septal defect was so situated that the aorta distinctly overrode the septum. The pulmonic stenosis, coupled with the tricuspid stenosis, resulted in a right to left shunt at the ventricular level, giving a complex physiologically reminiscent of cyanotic tetralogy of Fallot. However, the morphology of the left A-V (tricuspid) valve and the inflow tract of the morphologic right (left-sided) ventricle differed markedly from tetralogy. Likewise, the relationship of the arterial trunks was that of complete inverted transposition.

TABLE IV

Anatomic Details of Thirteen Cases of Mixed Levocardia

Case No.	Sex, Age (yr.)	Position of Arterial Trunks	Origin of Coronary Arteries	Position of A-V Valves	Pathologic Complex	Right Atrium
					A. Eight Cases of Type IA	
1	M, 14	Aorta anterior and to the left; pulmonary posterior and to the right	Right-sided coronary from right anterior sinus; left-sided coronary from posterior	Correspond to distal chamber	Insufficiency of left A-V valve	Hypertrophy and dilatation
2	M, 22 mos.	Aorta anterior and to the left; pulmonary posterior and to the right	Right-sided coronary from right anterior sinus; left-sided coronary from posterior	Correspond to distal chamber	Coarctation of the aorta with anatomic aortic stenosis and abnormal left A-V valve	Hypertrophy and dilatation
3	M, 14	Aorta anterior and to the left; pulmonary posterior and to the right	Right-sided coronary from right anterior sinus; left-sided coronary from posterior	Correspond to distal chamber	Coarctation with Ebstein's anomaly of the left A-V valve	Hypertrophy and dilatation
4	M, 12	Aorta anterior and to the left; pulmonary posterior and to the right	Right-sided coronary artery from right anterior sinus; left-sided coronary from posterior	Correspond to distal chamber	Ventricular septal defect and left A-V valve stenosis	Hypertrophy and dilatation
5	F, 2	Aorta anterior and to the left; pulmonary posterior and to the right	Right-sided coronary artery from right anterior sinus; left-sided coronary from posterior	Correspond to distal chamber	Ventricular septal defect and abnormal left A-V valve	Hypertrophy and dilatation
6	F, 16	Aorta anterior and to the left; pulmonary posterior and to the right	Right-sided coronary from right anterior sinus; left-sided coronary from posterior	Correspond to distal chamber	Ventricular septal defect with pulmonic stenosis and abnormal left A-V valve	Hypertrophy and dilatation
7	F, 14	Aorta anterior and to the left; pulmonary posterior and to the right	Right-sided coronary artery from right anterior sinus; left-sided coronary from posterior	Correspond to distal chamber	Ventricular septal defect, pulmonic stenosis, overriding aorta, and left A-V valve stenosis	Hypertrophy
8	M, 6 mos.	Aorta anterior and to the left; pulmonary posterior and to the right	Right-sided coronary from right anterior sinus; left-sided from posterior	Correspond to distal chamber	Complete transposition with overriding aorta and pulmonary atresia (pseudotruncus complex)	Hypertrophy
					B. Two Cases of Type IB	
9	M, 4 wks.	Vessels emerge side by side; aorta to the right; pulmonary to the left	Right-sided coronary from left anterior sinus; left-sided coronary from posterior sinus	Correspond to distal chamber	Fetal coarctation with ventricular septal defect	Hypertrophy and dilatation
10	F, 12	Aorta anterior and to the right; pulmonary posterior and to the left	Right-sided coronary from left sinus; left-sided coronary from right posterior sinus	Correspond to distal chamber	Pulmonary stenosis and ventricular septal defect	Hypertrophy
					C. One Case of Type II	
11	M, 19	Aorta anterior and to the right; pulmonary posterior and to the left	Right-sided coronary from right posterior sinus; left-sided coronary from left posterior sinus	Correspond to distal chamber	Pulmonary stenosis and ventricular septal defect	Hypertrophy and dilatation
					D. Two Cases of Type III	
12	F, 8	Aorta anterior and to the right; pulmonary posterior and to the left	Right-sided coronary from right posterior sinus; left-sided coronary from left posterior sinus	Correspond to distal chamber	Anatomic Taussig-Bing heart with Ebstein's anomaly	Hypertrophy and dilatation
13	M, 5 wks.	Aorta anterior and to the left; pulmonary posterior and to the right	Right-sided coronary from right posterior sinus; left-sided coronary from left posterior sinus	Correspond to distal chamber	Partial inverted transposition with pulmonary stenosis	Atrophy

TABLE IV *Continued*

Pulmonic Ventricle	Left Atrium	Aortic Ventricle	Abnormal Venous Return	Other Cardiac Anomalies	Other Organ Anomalies
(with complete inverted transposition)					
Hypertrophy and dilatation	Hypertrophy and dilatation	Hypertrophy and dilatation	Entry of coronary sinus into left atrium	Patent foramen ovale	Multiple accessory spleens; heterotropic pancreatic ducts
Hypertrophy and dilatation	Hypertrophy and dilatation	Normal	Persistent left superior vena cava entering the coronary sinus	Patent foramen ovale	None
Hypertrophy and dilatation	Hypertrophy and dilatation	Hypertrophy and dilatation	None	Patent foramen ovale	Details not available
Hypertrophy and dilatation	Hypertrophy and dilatation	Atrophy	Persistent left superior vena cava entering coronary sinus	None	None
Hypertrophy and dilatation	Hypertrophy and dilatation	Hypertrophy and dilatation	None	Patent foramen ovale	None
Hypertrophy and dilatation	Hypertrophy and dilatation	Hypertrophy and dilatation	None	Bicuspid pulmonic valve	None
Hypertrophy	Normal	Atrophy	None	Bicuspid pulmonic valve	None
Hypertrophy	Normal	Normal	None	Patent foramen ovale and patent ductus arteriosus	None
[with complete (noninverted) transposition]					
Hypertrophy	Normal	Hypertrophy and dilatation	None	Widely patent ductus arteriosus	Congenital defect of right diaphragm; malformed kidneys; double left ureter; absence of gallbladder
Hypertrophy	Normal	Normal	None	Atrial septal defect created artificially at age of 2½ yrs.	None
(with complete transposition)					
Dilated	Hypertrophy	Hypertrophy and dilatation	Right pulmonary veins, right superior vena cava and azygos vein—morphologic left atrium; left pulmonary veins, left superior vena cava, inferior vena cava, and coronary sinus—morphologic right atrium	Right aortic arch	Inversion of lungs, liver, spleen, stomach and intestines
(atria and ventricles wrongly connected)					
Hypertrophy	Hypertrophy and dilatation	Atrophy	None	None	None
Morphologic right ventricle leading to pulmonary trunk and aorta; hypertrophy and dilatation	Hypertrophy and dilatation	Morphologic left ventricle leading through ventricular septal defect to morphologic right ventricle; atrophy	Right pulmonary vein—right atrium; left pulmonary veins, left superior vena cava, right superior vena cava, inferior vena cava and coronary sinus—left atrium	Atrial septal defect (secundum type); absent eustachian and thebesian valves; right aortic arch	Inversion of the liver, stomach and spleen; atresia of the ileum; malrotation of the colon; bilobed spleen

6. Overriding conus (aorta) and pulmonary atresia (pseudotruncus) complex (Case 8, Figs. 19, 20, 21). This is a type of complete inverted transposition, although there is pulmonary atresia. Our point of reference is the position of the arterial trunks or their remnants with respect to each other; thus, this is an extension of Case 7. All other features of mixed levocardia with ventricular inversion are present.

7. Coarctation of the aorta with anatomic aortic stenosis and abnormal left A-V valve (Case 2, Figs. 4, 5, 6). It is difficult to evaluate the nature of this coarctation. The right side of the heart is hypertrophied; therefore, pulmonary hypertension must have been present. This may, therefore, correspond to a fetal or transitional type of coarctation. It cannot be stated with certainty that there is left A-V (tricuspid) valve insufficiency, for on the one hand there is hypertrophy and dilatation of the left atrium, and on the other a normal left-sided ventricle. The aortic stenosis is diagnosed as anatomic since the left-sided (aortic) ventricle is not hypertrophied and hence there is no evidence of physiologic stenosis.

8. Coarctation of the aorta with Ebstein's anomaly of the left A-V valve (Case 3, Figs. 7, 8) The left A-V valve presented features of both downward displacement and irregular formation and adhesion to the wall of the right ventricle. In view of the fact that this was occurring in the aortic ventricle, the complex produced is quite different than in Ebstein's complex in normal levocardia. In our case, there is hypertrophy of all chambers of the heart, as in left A-V valvular insufficiency. The coarctation is difficult to categorize here. In view of the hypoplasia of the ascending aorta, and the lack of clinical evidence of an obstructive lesion in the aorta, the pathologic findings bear some resemblance to fetal coarctation.

Summary of Complexes in Type IA: It is thus clear that our series of mixed levocardia with ventricular inversion and complete inverted transposition of the arterial trunks, together with a review of the literature, show anomalies and complexes which are anatomically and, in some cases, physiologically similar. The basic abnormality appears to lie in the left A-V valve, which may show stenosis, insufficiency or Ebstein's malformation. Associated with this there may be abnormalities in the inlet of the right ventricle. The abnormal left A-V (tricuspid) valve may be associated with ventricular septal defect, and the latter in turn with pulmonic stenosis. If, in addition, the aorta overrides and the pulmonic stenosis is severe, a type of cyanotic tetralogy of Fallot is present. Rarely, there is pulmonary atresia with pseudotruncus. The abnormal left A-V valve may be associated with hypoplasia of the aorta with coarctation. There appears to be a distinct flora of anomalies in this type of mixed levocardia; therefore, it is possible that these anomalies are basically related to inversion of the ventricles and the complete inverted transposition of the arterial trunks.

Type IB. Mixed Levocardia with Ventricular Inversion and Complete (Non-inverted) Transposition of the Arterial Trunks (Cases 9 and 10, Figs. 22, 23, 24): The external features of this type differ from those of type IA in the positions of the aorta and pulmonary trunk, and in the coronary origin and distribution. The aorta is situated to the right and somewhat anteriorly, and the pulmonary trunk is situated to the left and somewhat posteriorly (as viewed from the anterior surface of the heart) as in complete transposition without ventricular inversion. Although the right-sided coronary artery forms the anterior descending branch, in contrast to type IA, the right-sided coronary artery emerges from the left side of the aorta, either from the left anterior or left sinus of Valsalva. The left-sided coronary artery emerges from the posterior or right posterior sinus of Valsalva, and passes behind the pulmonary trunk, instead of in front of it as in type IA (Fig. 38).

Internally, the aorta emerges in part or completely from the right-sided (morphologic left) ventricle, and the pulmonary trunk from the left-sided (morphologic right) ventricle. The internal structure of the ventricular chambers in our two cases are not as altered as in type IA. The left- and right-sided A-V valves, which correspond to the distal chamber, are not as altered in morphology as in the previous type.

Since these are very rare hearts the various complexes possible are not known. One of our cases was the seat of complete transposition with ventricular septal defect and fetal coarctation and the other, complete transposition with ventricular septal defect and pulmonary stenosis. Although the aorta overrode the septum somewhat, the complex is still considered a type of complete transposition because of the relative positions of the arterial trunks.

Type II. Mixed Levocardia with Atrial Inversion (Case 11; Figs. 25, 26, 27, 28; Table IV): As previously shown, the venous return in these cases is usually into the morphologically correct atrium

situated in an inverted position. Our case and those of Platzer[21] and Ivemark[41] are exceptions. In our case, the right pulmonary veins, the right superior vena cava and the azygos vein entered the morphologic left (right-sided) atrium, while the left pulmonary veins, the left superior vena cava, the inferior vena cava and coronary sinus entered the morphologic right (left-sided) atrium. This was accompanied by a complex consisting of complete transposition, pulmonary stenosis, ventricular septal defect and right aortic arch. This case corresponds to the cases in the literature which show some type of transposition complex with right aortic arch and, like them, is a variety of isolated levocardia.

The cases in the literature and our case are examples of type IIB, from the standpoint of position of chambers and arterial trunks. In the usual cases where the venous return is to the morphologically correct atrium and the transposition is complete, then a type of "corrected" transposition may be said to be present. Theoretically, there should be a type IIA with atrial inversion and normal position of arterial trunks (Fig. 37); we do not know if such a case actually exists.

Type III. Mixed Levocardia with Atria and Ventricles in Almost Normal Position but Wrongly Connected (Cases 12 and 13, Figs. 29 to 36, Table IV): We have not been able to find this type in the literature. The external appearance of our two specimens is similar. The efferent vessels emerge from the right aspect of the ventricular mass. The right atrial appendage is displaced caudally and is not well seen on the anterior surface of the heart. The left atrial appendage on the other hand is seen prominently superiorly and anteriorly. The anterior descending coronary artery is seen in its usual position but arises from a main stem which travels horizontally from the base of the aorta. Internally, although the right atrium is situated anteriorly, it is also caudal and the left atrium, although situated posteriorly, is also cranial. The right atrium communicates with the left ventricle through a mitral orifice which is situated inferiorly and slightly to the right, while the left atrium communicates with the right ventricle through a tricuspid orifice which is situated superiorly and somewhat to the left, at the spot where we would expect an efferent vessel to emerge. The architecture of the right ventricle is disturbed in both cases, but the A-V valves are abnormal only in Case 12. The hemodynamic effects of this arrangement of chambers on the endocardium and valves cannot be surmised from our cases because of the severe complexes present and the small number of cases. Likewise, the flora of complexes in this type are not known. Case 12, anatomically, was the seat of a Taussig-Bing complex associated with Ebstein's complex of the left A-V (tricuspid) valve. Physiologically, it acted as a ventricular septal defect with overriding pulmonary trunk and Ebstein's complex of the left A-V valve. Case 13, anatomically, was the seat of a partial inverted transposition of the arterial trunks with pulmonary stenosis complex associated with abnormal venous drainage. Physiologically, the venous and arterial blood cirlations were mixed.

It is thus to be noted that our series of mixed levocardias present both inverted complete and inverted partial transposition, as postulated by Spitzer.[35]

Summary

1. The pathologic anatomy of thirteen hearts with mixed levocardia was studied.

2. The nomenclature in mixed levocardia of chambers, valves and coronary arteries is discussed. Atria and valves should be designated according to morphology and position. Ventricles should be designated according to their distal connections, in addition. Coronary arteries should be designated left- and right-sided.

3. The cases of mixed levocardia presented and those reviewed in the literature may be divided into type I, with ventricular inversion; type IA, with complete inverted transposition; type IB, with complete (noninverted) transposition; type II with atrial inversion; and type III, with relatively normally situated but wrongly connected chambers.

4. Type IA hearts have certain common external and internal morphologic characteristics and are associated with a spectrum of complexes consisting of combinations of left A-V valve abnormality—insufficiency, stenosis, or Ebstein's malformation; with ventricular septal defect, pulmonary stenosis or atresia, and coarctation of the aorta.

5. Types IB and III are rare.

6. Type II is one of the types of isolated levocardia with or without splenic abnormalities.

Acknowledgment

We are indebted to Drs. Joseph D. Boggs, Donald E. Cassels, Cecil A. Krakower and Robert W. Wissler for the use of their material.

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Historical Milestones

Coarctation of the Aorta (Robert Graham, 1814)

SAUL JARCHO, M.D.
New York, New York

A RECENT contribution to this series embodied two of the earliest descriptions of aortic coarctation, that by J. F. Meckel (1750) and that by M. Paris (1791).[1] Readers were able to observe the predominantly anatomic character of both presentations, the earlier of which contained also an elaborate superstructure of hemodynamic theory.

The report of Robert Graham, reproduced herewith, marks a further accretion of knowledge. The exact title is *Case of Obstructed Aorta. By Robert Graham, M.D. One of the Physicians to the Royal Infirmary, Glasgow.*[2]

* * *

ROBERT GRAHAM'S CASE (1814)

The case which I take the liberty of transmitting to the Medical and Chirurgical Society, has, as far as I know, but one parallel on record, and in it the appearances on dissection only are mentioned. No history is given of the case. I believe I have extracted from the books of the Infirmary, such parts of the reports taken at the patient's bedside as are of any importance, and have even noted some anomalous symptoms which may appear trifling, because it may perhaps be found that an improved state of knowledge may give importance to what at present seems adventitious and without value. I am sorry to say, that as I can see no diagnostic symptom, the occurrence of this derangement adds but another chance to our guessing wrong during life at the diseases of the heart.

Henry Frere, fourteen years of age, a weaver, admitted into the Infirmary, 3d August 1813, when the following history of his symptoms was entered on the journal of the house:

"Two weeks ago, after exposure to cold, was affected with dry cough, which for the last eight days has been attended with pretty copious expectoration, and pain impeding respiration, and excited by the cough in the left side of the chest; p. 100, pretty firm. Little appetite. Much thirst. Tongue rather white. Bowels regular. Sleeps ill. Sweats a good deal. Has used no medicines."

The disease was looked upon as a case of pneumonia, but of such standing that suppuration seemed to have taken place, and in which therefore no material benefit was likely to result from any treatment. However, under the ordinary means, bleeding, blistering, expectorants, and the free use of cathartics, I had the satisfaction of seeing the symptoms decline. The blood from the first bleeding was somewhat buffy. The pulse, however, generally ranged from ninety-two to one hundred and four, and is variously marked in the reports, full strong, sharp: it was always regular. The *sputum* became more copious, gross, and tinged with blood. He perspired chiefly on the upper parts of the body, moaned in his sleep, took little food. On the 8th, he was affected with nausea and vomiting. On the 19th, he had a febrile attack, which lasted a few days. On the 20th there was much pain in the left eyeball. On the 27th he complained only of palpitation, the first time that symptom is noticed in the journal, though I rather think this was an oversight. No report was taken from this date till the 6th of October, when he was dismissed from the hospital, "cured."

The palpitation had subsided as the strength increased, which encouraged a hope I was willing to entertain, that that symptom proceeded from weakness, though I could not but express fears that the inflammation had extended to the pericardium or heart. The uncertainty of the *diagnosis* in cases of this kind, is but too well known to every practitioner.

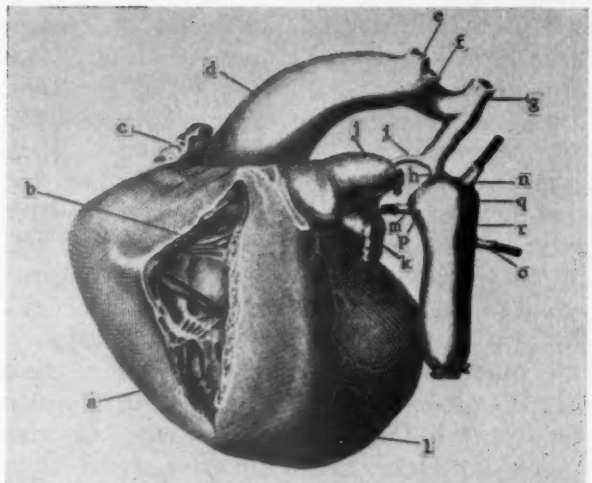

Fig. 1

FIG. 1. A, the right ventricle slit open, and gaping from a piece of bougie placed in it. B, the tricuspid valve, with the opening from the auricle. C, part of the right auricle. D, the dilated portion of the aorta. E, the enlarged arteria innominata, puckered from a ligature having been passed round it when the vessel was injected. F, the left carotid, of its natural size. G, the left subclavian greatly enlarged, immediately below which the aorta is seen much contracted, as far as H, where it is impervious. I, the canalis anteriosus. J, the pulmonary artery. K, part of the left auricle. L, the left ventricle. M, N and O, the enlarged intercostals entering the aorta below the stricture. P, Q and R, three smaller vessels torn off short.

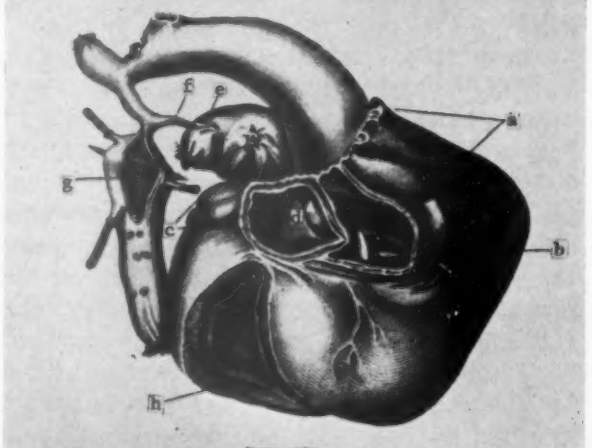

Fig. 2

FIG. 2. Shews the opposite side of the preparation. A, the right auricle, with its opening into B, the right ventricle. C, the left auricle. A portion of each auricle is cut away, and in the partition between them is seen, at D, the site of the foramen ovale. E, the pulmonary artery tied just beyond its division. F, the canalis arteriosus. G, an incision, into the aorta from the stricture to the second pair of intercostals, one of which that is not materially enlarged, it enters. The incision is kept open by a piece of whalebone, which passes through the sides of the vessel. Three pairs of intercostals, of about the natural size, but torn off short, are seen lower down. H, the left ventricle, with its thickened walls cut open, and held aside by a bougie.

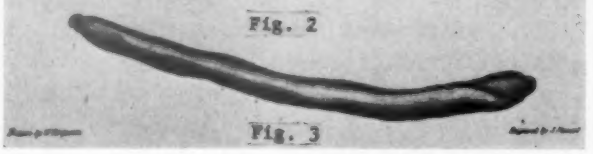

Fig. 3

FIG. 3. A portion of the mammary artery after injection, merely to shew the increase of its size.

I was inclined to suspect the effusion of serum within the pericardium, or perhaps adhesions of the heart to its capsule, though I had seen at least two cases about that time of the most intimate and general adhesion, without the circulation having been in any degree affected.

These fears were much strengthened by the boy's appearance on returning to the hospital, on the 13th November, when the throbbing of the carotid and subclavian arteries was very remarkable. On his readmission, the following report appears on the journal:

"13th November, dyspnoea, palpitation at the heart, and pain in the left side of the thorax returned soon after he left the house, and have been gradually increasing. P. 88, regular. Appetite pretty good. Considerable thirst. Bowels kept open by physic. Received temporary relief from the application of a blister."

Blisters and cathartics were again employed, and the symptoms for a time declined. The pain which had been removed, returned to the left side of the chest, on the evening of the 29th. A blister was repeated next day which gave much pain, till he was suddenly seized with a febrile attack on the 2d December, when the part became quite easy. There was no strangury. The fever was gone next day. A similar attack, accompanied with nausea and vomiting, was experienced on the 12th, and immediately removed by the operation of an emetic. He had acidity at stomach and cardialgia after meals. On the 23d he is reported as having been affected for ten days with pain in the right side of the chest, increased by motion, and by full inspiration; and by frequent cough, most troublesome in the night. The pulse had again risen. He was blistered, used cathartics, and was twice bled, the blood, especially after the first operation, being very buffy. The pulse came down, and the pain was removed, but the cough and palpitation continued. The

circulation was again quickened on the 27th, and remained hurried till his death: he sunk in strength; was drenched in perspiration; took no food; was attacked with frequent vomiting; the urine became scanty; his sleep was disturbed; the dyspnoea and palpitation increased; and he expired about noon on the 2d of January. The pulse, while he was last in the hospital, fluctuated from ninety to one hundred and sixteen, and was of various degrees of strength and firmness; latterly only, weak: it was always regular.

Dissection. There was nearly a pound of serum in the cavity of the abdomen, and the bowels were distended with flatus, but the viscera seemed natural. Immediately on turning up the sternum, the pericardium presented itself, very much enlarged, obscuring the left lung, and adhering to the *pleura costalis*. This capsule, which was thin and beautifully transparent, contained about an ounce of fluid, and a heart nearly twice the natural size, for a boy of this subject's age. The arteries and trachea were divided above the arch of the aorta, the contents of the thorax torn downwards, and the aorta being divided below, the whole was removed from the body. The walls of the left ventricle were about an inch in thickness, but no other derangement in the structure of the heart, or its valves, was observed. (Figs. 1 and 2.) The capacity of the cavities seemed natural. The aorta expanded unusually near its origin, so as to form a kind of pouch, but after giving off the branches to the head and superior extremities, its diameter was praeternaturally contracted. It was continued of this diminished size, till after its union with the *canalis arteriosus*, where it was completely impervious. The coats were not thickened, or in any way diseased, except that about half an inch below the stricture, there was a smooth elevation of the inner surface, less raised, but having nearly the diameter of a split pea; otherwise the appearance was exactly such as if a ligature had been tied tightly around the artery. It is faithfully represented in the drawings. The obstruction was about a line in breadth. The artery then received three trunks about the size of crow quills, and near them three smaller ones, afterwards resuming its natural size along the *vertebrae*. These three trunks are evidently the uppermost of the inferior intercostals. Their coats were remarkably thin, like those of veins. A probe passed from the pulmonary artery along the *canalis arteriosus*, to the obstructed portion of the aorta, but from its thickened appearance it did not seem probable much communication by means of it could have been allowed, and the florid countenance of the body during life establishes the same conclusion. There having been no suspicion of this singular deviation from the natural structure, till after the contents of the thorax were removed from the body, it was impossible to trace with the accuracy that could be wished, the anastomosing branches by which the circulation had been carried on in the inferior parts of the body; but I think enough has been observed to lead us very near the truth. The *arteria innominata*, the left subclavian, the superior intercostals, and the mammary arteries were much enlarged (Fig. 3). The epigastric was reported of its natural size.*

These facts, and the aorta acquiring at least very nearly its natural size immediately below the stricture,† shew that the blood did not pass to the inferior extremities, in any material quantity, as might perhaps have been expected, by the inoculations of the mammary and epigastric arteries, but chiefly by the communications of the superior intercostals and the mammary arteries, with the three large branches entering the aorta below the stricture: also from the mammaries and thoracics through others of the intercostal and diaphragmatic arteries.

The lungs were very light coloured; the left lobe much collapsed. In each side of the

* I regret that having been obliged to leave the hospital immediately after the visit, I was not present at the inspection of the body, but the authority of the report sustains no loss by having been left to the intelligence and zeal of Messrs. Rainy, Wilson, and McKenzie, the resident clerks to the house, who performed the dissection. Except the epigastric artery, which it was not thought necessary to preserve, I have since repeatedly examined all the parts connected with the circulation. The whole are now beautifully preserved in the Museum of my friends Drs. Robertson and Monteath. The greatest external circumference of the aorta, near its origin, measured 3.8 inches. The left subclavian 1.3 inch. The aorta immediately after the left subclavian was given off 0.8 of an inch; and immediately below the stricture 1.6 inch.

† Dr. Monteath doubts whether the abdominal aorta is quite as large as natural. The branches given out by it were unfortunately cut off so short, that the tying of them in order to inject the portion of the artery preserved has necessarily lessened its diameter, and to this I am inclined to attribute the whole of the diminution. The measurements I have given were made before injecting, and will enable any one to determine the question by comparison with other cases.

thorax there was a small quantity of bloody serum.

Remarks. The first question that naturally arises on reading the account of the dissection, is to ascertain whether this uncommon appearance of the aorta was a congenital formation, or the result of diseased action. On the first inspection of the parts, I was led, from the limber and healthy appearance of the coats of the stricture, to believe that the appearance was a connate *lusus naturae*, and thought to get some information from the boy's friends, of his state, especially during infancy, with a view to decide this. I have been disappointed, however, in every inquiry I have made. He had only been in Scotland five weeks before he came under my care, and I have been able to procure but imperfect information. No one knows any thing about him previous to the time he came to Glasgow. At that time, I am told, he seemed free from complaint, was active, and without dyspnoea, or any apparent uneasiness, at his sports. He was stoutly made, particularly about the chest. He was also well limbed. He had a fair complexion and dark brown hair. The presumption, therefore, is that there was no original derangement in the arterial system, and a careful inspection of the parts, an attentive consideration of the case, and reflection on similar and analogous instances, will present a view which gives much countenance to the opinion of the blood having but recently been diverted from the natural channel.

I believe, it is found that in the deviations of nature from the ordinary structure, she seldom destroys the function of an organ, without enabling another to carry it on, and in many instances with little imperfection. I mean, of course, to except those monsters in which she disregards all rule, and which cannot live after birth. In this case, however, although there was never any deficiency of blood circulated in the lower extremities, yet the enlarged and thickened heart, and the increased diameter of the aorta at its origin, seemed to shew that there had been much resistance to the transit of that fluid; also that vessels of sufficient diameter readily to supply the place of the aorta, had not been originally furnished by nature.‡ And does not the thinness of the coats of the enlarged intercostal arteries, shew that they have been under the influence of distension from praeternatural impulse? It may be presumed, that if this had existed as a mal-conformation from infancy, the vessels would have long before recovered their natural structure. Nor indeed is it in infancy only, that attempts must have been made to repair this imperfection, for, if it had been *lusus naturae*, it must, even *in utero*, have opposed a barrier to the circulation of the whole mass of blood, as it was placed below the *canalis arteriosus*.

I think it a subject even of some practical importance to determine this point. If we find that the structure is the consequence of disease, we add, in the first place, another case to prove, that even where the great artery of the body is obliterated, there is no risk from defective circulation in the parts below, and therefore the surgeon may be emboldened to tie any artery within reach of his knife, without fear about the transmission of the blood; and, secondly, we are taught that there may exist in the arterial system, or part of it, a disease having this effect, and yet compatible with life.

I. The first point has, I think, been long since established. There are several cases on record, of obstructions, from various states of disease, in different parts of the aorta, which must have admitted the passage of at most only a very small quantity of blood: as that related by Stenzel, (*Dissertatio de steatomatibus aortae*); two cases by Meckel, (*Mem. de l'Acad. R. de Berlin*, 1756); that by Stoerk, (*Ann. Med.* II. p. 171). Mr. Cooper tied the abdominal aorta of a dog, without material detriment to the circulation, (*Medico-Chirurgical Transactions*, Vol. II. p. 258). In the Museum belonging to Messrs. Pattison and Russel, there is a preparation where the aorta

‡ I know that the heart is frequently much enlarged and thickened without any difficulty to the transmission of the blood; but this is a disease of much slower progress. Within these two days, I have seen such a case terminate fatally with symptoms wonderfully similar to those of Frere. There were the same palpitations and throbbing in the neck; the same rapid pulse, for the most part sharp and regular; the same repeated attacks of fever and pain of chest requiring venaesection and the other branches of the antiphlogistic regimen; the same accessions of nausea and vomiting. Dissection shewed general and firm adhesions of lungs, otherwise healthy, to every thing in contact with them, and a monstrously enlarged heart, everywhere firmly united to a thickened pericardium, except at a small spot near the apex. The walls of all the cavities, particularly of the ventricles, were very much thickened, those of the left ventricle measuring more than an inch. The capacity of the auricles only was enlarged, but that greatly. Polypi were contained in several of the cavities, but having the appearance of those formed after death. The disease was of five years standing: the subject, a girl of about seventeen years of age.

is plugged up, by a laminated coagulum, just above the bifurcation of the iliacs, into both of which this substance extends. It is impossible to say from inspecting the preparation, whether the recent artery were absolutely impervious; and unfortunately, though Mr. Pattison at my request has kindly examined the papers of the late Mr. Allan Burns, to whom the preparation belonged, he has been unable to find any account of the case. The case which most nearly resembles that of Frere, is one which occurred in the Hôtel Dieu. The appearances on dissection are detailed by M. Paris, in Desault's Surgical Journal. The artery was not in it quite closed, and as the state of the heart is not mentioned, it ought perhaps to be presumed natural, otherwise there is no material difference in the cases. The identity of the site of the stricture is deserving of notice, lest after examples should prove a peculiar tendency toward its formation in this portion of the vessel. Analogy is in favour of such a supposition, definite portions of continuous and similar structures, being in many instances liable to particular diseases. It is a matter of great regret, that in the case of M. Paris, no account whatever is given of the symptoms that occurred during life. It is indeed difficult to say why morbid appearances are recorded at all, where there is no previous history, as they can be productive of little or no instruction.

II. When it was believed essential to the production of adhesive inflammation within an artery, to retain the sides in contact, it must have been very difficult to believe, that obliteration of the aorta by its means, could take place where there was evidently no pressure applied to the artery; but we now know that a vessel may be converted into a ligamentous cord, by an injury which does not at the moment interrupt the circulation through it. This is proved by Morand's case (*Mém. de l'Acad. R De Paris*, an. 1736), where the artery was closed by a violent contusion; and still more unequivocally by Jones's experiments (Jones on Haemorrhage). The Society will recollect instances on record, though I cannot at the moment refer to them, where on dissection both arteries and veins have been found obliterated without any evident cause. It seems likely, that, in such cases, the obstruction had arisen from the same modification of diseased action as occurred in Paris's case, and in my own; but the vessels being only of secondary importance, their loss did not destroy life. The obliteration was of small extent in the case I have related, which is to me a convincing proof that it was recent. Though ultimately obstruction of the flow of blood through an artery, causes it to close as far as the next anastomosing branch, yet this is comparatively a slow process, and not effected till after the vessel is shut at the diseased point. It will easily be believed, therefore, that in this case the narrowed diameter of the trunk of the aorta, from the left subclavian to the stricture, was a stage in its progress to complete obliteration, arrested only by the death of the boy. And though there is every reason to believe that this morbid affection was *recent*, it seems equally evident, that it could not have been *sudden*. The increased muscular substance of the heart, as well as the enlargement of the aorta, must have been a work of time. And the existence of life under so great an interruption to the vital operations, may be considered as a proof and example among many others of the wonderful power of nature in accommodating herself to the greatest changes in the most essential organs of life, provided such changes are slow and gradual, and provided the action of the organs is not hurried, disturbed, or overexcited. The disturbance in this case consisted in the accidental catching of cold, producing catarrhal fever. The practical inferences from this are obvious, for it is clear, that under this, and all other incurable organic lesions of vital parts, life can be protracted and suffering alleviated, only by avoiding exposure, fatigue, emotions of mind, and stimulating diet.

* * *

Author's Comment on Graham's Report

Unlike Meckel and Paris, who were anatomists and whose studies of coarctation were presented earlier in the present series,[1] Robert Graham was primarily a clinician and he envisioned the problem of coarctation in clinical terms. His report is really an attempt to establish diagnostic criteria for the disease. Accordingly he presents the clinical history in considerable detail and censures the earlier authors for having disregarded the clinical aspects of the problem. He says, "It is a matter of great regret, that in the case of M. Paris, no account whatever is given of the symptoms that occurred during life. It is indeed difficult to say why morbid appearances are recorded at all, where there is no previous

history, as they can be productive of little or no instruction."

In contrast to the detailed clinical history, the report of physical examination is meager and consists almost entirely of external inspection, plus measurement of the pulse rate. Despite the work of Auenbrugger and Corvisart there is no mention of percussion.

Aside from marked throbbing of the carotid and subclavian arteries Graham noted nothing distinctive. He concluded, with admirable frankness, that since he could see no diagnostic symptom, or as we should say, no pathognomonic sign, "the occurrence of this derangement adds but another chance to our guessing wrong during life at the diseases of the heart."

Dissection revealed total occlusion of the aortic lumen in the region of the ductus; the latter channel was patent but narrow. The aorta showed prestenotic dilatation. The anastomoses are described adequately. From the size of the various anastomotic channels Graham concluded that the lower extremities derived their principal blood supply, not through a connection between the mammary and epigastric arteries, but from other anastomoses, which he describes in detail.

From the fact that the patient had been active before his final illness Graham judged that the lesion could not have been present since birth. Yet the healthy appearance of the aortic lining at the site of stricture pointed to the absence of recent disease. He concluded that the blood had been "but recently diverted from its natural channel."

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Case Reports

Ebstein's Malformation of the Left Atrioventricular Valve in Corrected Transposition, with Subpulmonary Stenosis and Ventricular Septal Defect*

L. H. S. VAN MIEROP, M.D.,† RALPH D. ALLEY, M.D., F.A.C.C., HARVEY W. KAUSEL, M.D.
and ALLAN STRANAHAN, M.D.
Albany, New York

THE PURPOSE of this paper is to report an example of Ebstein's malformation of the left atrioventricular valve in association with corrected transposition of the great vessels, subpulmonary stenosis and ventricular septal defect. Classically Ebstein's anomaly involves the right atrioventricular valve in normally oriented hearts. It consists of a congenital downward displacement of the septal and posterior leaflets of the tricuspid valve, resulting in atrialization of the proximal right ventricle. To our knowledge the literature contains only three examples of Ebstein's anomaly occurring on the left side of the heart; all three were associated with corrected transposition of the great vessels. Two of these were recognized and reported by Edwards and associates.[1,2] Their second case also had a ventricular septal defect. The third case was discovered through the accurate anatomic description of a case in Kernan's series of corrected transposition.[3] We have had the privilege of examining this specimen and confirm the presence of left Ebstein's anomaly with corrected transposition and a surgically closed high ventricular septal defect.

In "complete transposition" the great vessels are transposed but the cardiac chambers are normally oriented. The aorta originates from the right ventricle and runs anterior and parallel to the pulmonary artery which arises from the left ventricle. In "corrected transposition" the aorta and pulmonary artery are likewise transposed in their relationship but each takes origin from the correct side of the heart. In addition, the two ventricles are inverted; i.e., the right ventricle internally resembles a normal left ventricle and the left ventricle a normal right ventricle. The left atrioventricular valve, therefore, is tricuspid and its attachments are similar to those of a normal tricuspid valve. Hence, it would appear logical that Ebstein's anomaly, when occurring on the left side of the heart, will always be found in association with corrected transposition.

CASE REPORT

Clinical Features: The patient was a fifteen year old boy with a history of cyanosis since birth. A heart murmur was first noted at eighteen months of age. He was always small for his age. Increasing cyanosis and incapacitation was alleviated for a time by a left Blalock shunt established at six years of age. The surgeon suspected the presence of a

* From the Subdepartment of Thoracic Surgery, Albany Medical College, Albany, New York. Supported by project H-1927, U. S. Public Health Service, and the Joint Fund for Medical Education contributed by affiliates of the New York State Heart Assembly, Inc., and State Committee on Tuberculosis and Public Health of the State Charities Aid Association.

† Present address: Montreal, Canada.

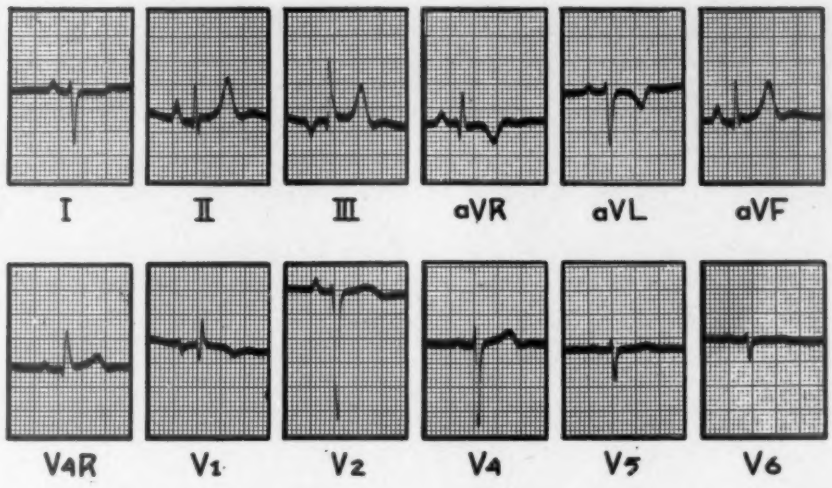


FIG. 1. Preoperative electrocardiogram showing right atrial and right ventricular hypertrophy. The change in the direction of the P wave when the limb leads were recorded was attributed to a wandering pacemaker.

transposition complex. During the three years prior to admission severe cyanosis and diminishing tolerance to exercise led the family to seek further surgical help.

On examination the boy was underdeveloped, cyanotic and exhibited clubbing of fingers and toes. The blood pressure was 100/80 mm. Hg in the right arm; the pulse rate was 100 per minute. The chest was symmetrical. A systolic thrill was palpated over the left third intercostal space parasternally. A harsh grade 3 systolic murmur was heard over the same area and the adjacent fourth interspace. The second sound over this area was snapping, pure, and was thought to represent an aortic second sound. No diastolic murmur was audible.

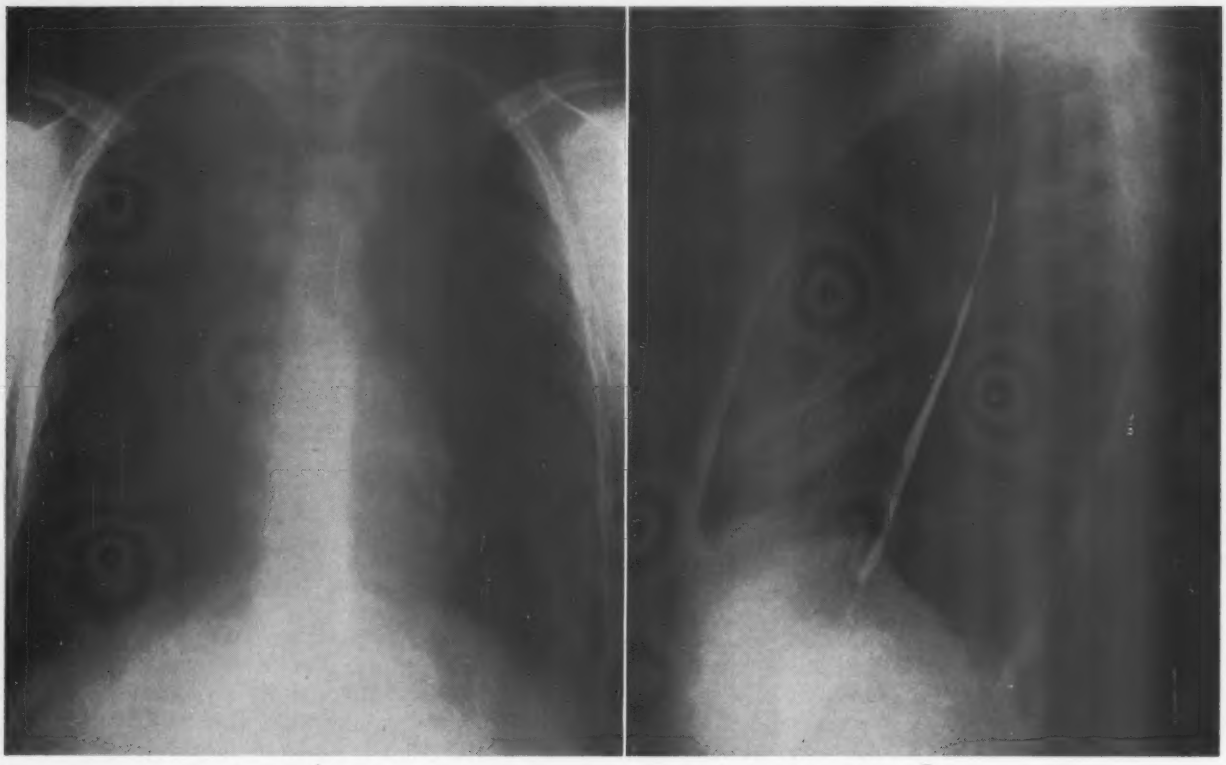
The hemogram revealed a hemoglobin of 22 gm. per cent, the hematocrit was 62 per cent. The *electrocardiogram* displayed a wandering atrial pacemaker, and was interpreted as indicating right atrial and right ventricular hypertrophy (Fig. 1). *Fluoroscopy and roentgenography* revealed the heart to be normal in size and shape, except for narrowing of the vascular pedicle and slight bulging of the left upper cardiac border (Fig. 2). No specific enlargement of the chambers was detected. The pulmonary vasculature was interpreted to be moderately decreased.

Venous cardiac catheterization was performed without incident. The catheter was advanced from the right ventricle into the pulmonary artery and also through a ventricular septal defect into the aorta and its innominate branch. A pulmonary stenosis was demonstrated. With the catheter in the aorta the patient was rotated and the relationship of the great vessels was misinterpreted as being normal. Hence, with a preoperative diagnosis of tetralogy of Fallot, exhibiting an unusual cardiac silhouette, corrective surgery was recommended.

Operative Findings: The anterior mediastinum was entered through a median sternotomy incision. Upon opening the pericardium the patient was found to have a corrected transposition. The pulmonary artery trunk was dilated, situated posterior and slightly to the right of the aorta, and exhibited a coarse thrill. Digital exploration of the right atrium revealed an intact atrial septum. Anticipating a left ventricular internal configuration, the right ventricle was similarly explored through the right atrioventricular valve to determine the position of the anterior papillary muscle and avoid injury to it in carrying out the ventriculotomy. A loose ligature was placed about the Blalock shunt, which although small, was patent. Catheters were passed into the venae cavae through the right atrial appendage and the right femoral artery was cannulated in preparation for bypass. A catheter was placed in the left atrium to aspirate the bronchial artery flow during bypass.

Upon placing the patient on bypass, the Blalock shunt was occluded, the patient's body temperature was lowered to 28°C. by means of a heat exchanger, and a right ventriculotomy was performed. The size of the ventriculotomy was restricted by the anomalous distribution of the branches of the coronary arteries and the position of the anterior papillary muscle (Fig. 3). The thickness of the right ventricular wall relative to its small lumen and the deep situation of the subvalvular stenosis and ventricular septal defect also contributed to the difficulties in exposure.

Examination of the right ventricle revealed an area of subpulmonary stenosis which resembled the ring-like structure typical of subaortic stenosis. Just beneath this area a 2 by $1^1/_2$ cm. ventricular septal defect was found. Despite the inadequate exposure, the subvalvular stenosis was largely resected. During resection of the posteromedial portion of it, a small opening was made into the left atrium requiring repair with a mattress suture. The ventricular septal defect was then closed



A B

FIG. 2. Posteroanterior (A) and left lateral (B) roentgenograms of the chest. Note the absence of left atrial enlargement.

with interrupted silk sutures. A reduction of systolic gradient across the pulmonary valve from 70 to 30 mm. Hg was demonstrated by measurements of pressures at the time of surgery.

After closure of the ventriculotomy, rewarming of the patient was started and the heart, which had started to fibrillate during the intracardiac procedure, was defibrillated with a single electric shock. A complete A-V heart block with slow ventricular rate was present. Internal electrodes were introduced and the patient placed on the pacemaker. After the patient was taken off bypass, the blood pressure rapidly returned to preoperative levels.

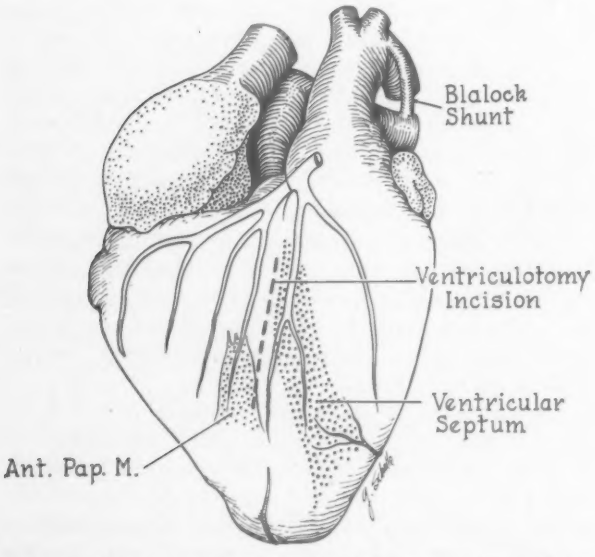


FIG. 3. Semidiagrammatic drawing of the heart of the case presented, showing the unusual distribution of the right coronary artery branches. The positions of the right anterior papillary muscle and the ventricular septum are indicated by stippling.

At the end of the procedure the patient was awake and talking, but was moderately cyanotic. There was no postoperative bleeding. His postoperative course was characterized by progressive fall in blood pressure, restlessness, tachypnea, increasing cyanosis, peripheral venous distention and coma. The patient died the evening of the first postoperative day.

Anatomic Findings (*Figs. 4 and 5*): At autopsy the heart weighed 360 gm. The apex was on the left and formed by the right ventricle. The venous end of the heart was normal. The aorta and pulmonary artery were transposed, the former was located anteriorly and somewhat to the left. The dilated pulmonary artery was situated behind and slightly to the right of the aorta. The internal structure of the right atrium was normal; there was a probe-patent foramen ovale. The right atrioventricular valve was bicuspid. The interior of the right ventricle resembled that of a left ventricle and its myocardium measured 18 mm. in thickness. The outflow of this chamber was partially obstructed by the ragged

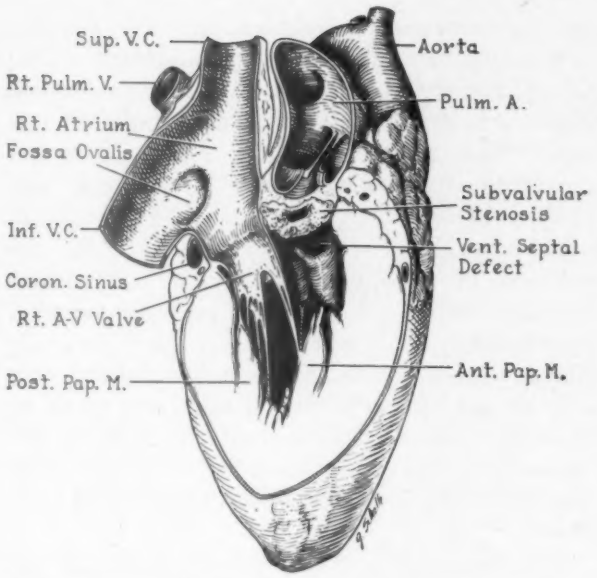


FIG. 4. View of the right side of the cardiac septum. The anterior portion of the medial leaflet of the right atrioventricular valve has been removed to show the subpulmonary stenosis and ventricular defect as they appeared at the time of surgery prior to correction.

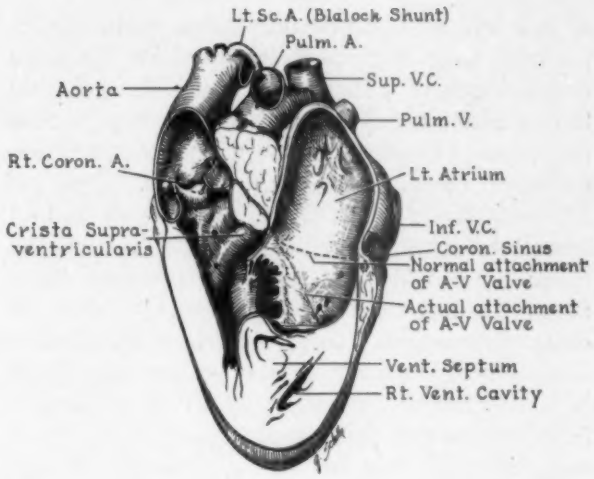


FIG. 5. View of the left side of the cardiac septum. Note the small size of the nonatrialized left ventricular cavity. The ventricular septal defect is hidden behind the anterior portion of the medial leaflet of the left atrioventricular valve.

fibrous remains of a subpulmonary stenosis, having the appearance of the usual subaortic stenosis. Just below this fibrous ring a surgically closed ventricular septal defect was present. The combination of right ventricular outflow obstruction and ventricular septal defect caused the marked cyanosis during life. The course of the circulation was comparable to that occurring in tetralogy of Fallot. The pulmonary valve was distorted due to elongated commissural attachments but was tricuspid, competent and not stenotic.

The left atrium was not enlarged and the pulmonary veins were within normal limits. The endocardium appeared thickened. The anterior leaflet attachments of the left atrioventricular valve were similar to those of a normal tricuspid valve. The septal and posterior leaflets were fused to the ventricular wall for a distance ranging up to 3 cm. below the annulus fibrosus. The orifice was not stenotic and there was no anatomic evidence of the presence of insufficiency during life. The portion of the left ventricle which was not atrialized was small and resembled a right ventricle in a normally oriented heart. The wall measured 12 mm. in thickness.

The coronary arteries originated from the right and left posterior sinus of Valsalva. The anterior wall of both ventricles was supplied by branches of the right coronary artery. The remainder of the heart, including the apex, was supplied by the left coronary artery.

COMMENTS

The occurrence of Ebstein's anomaly on the left side of the heart is of great anatomic interest, especially in view of the fact that only three previous cases have been reported. As stressed by Edwards, this anomaly characteristically involves the right atrioventricular valve. Hence, it is not surprising that when it occurs on the left side of the heart it is present in association with corrected transposition. In the case which is the subject of this report a subpulmonary stenosis and ventricular septal defect were also present. Failure to recognize the relative positions of the great vessels during cardiac catheterization lead to an erroneous diagnosis of tetralogy of Fallot. Undoubtedly, this error would have been recognized had the catheterization been supplemented by angiocardiography.

Reference is made to Anderson et al.[4] for a thorough general exposition of the anatomic and clinical features of corrected transposition of the great vessels, based on an experience with seventeen cases. These authors point out that the anomaly is more common than generally realized and is almost invariably accompanied by other cardiac defects. The importance of recognizing the presence of corrected transposition lies in the great anatomic handicaps it imposes upon the surgical attempt to correct intracardiac abnormalities which in the absence of corrected transposition would offer no special difficulty. As a corollary, the discovery of associated defects which render the case inoperable is of equal importance. A left Ebstein's anomaly is presently in this category.

The more commonly associated abnormalities

of the left atrioventricular valve occurring in patients with corrected transposition produce insufficiency of a degree to cause recognizable left atrial enlargement. It is noteworthy that the previously reported left Ebstein anomalies also exhibited left atrial enlargement. One of Edwards' cases of left Ebstein's anomaly had an associated ventricular septal defect, and the other patient had no associated defect other than the corrected transposition.[1,2] In these cases, presumably, the pulmonary blood flow was within normal limits or increased. It is conjectured, therefore, that our patient failed to exhibit left atrial enlargement externally in part because of the presence of pulmonary stenosis and diminished pulmonary blood flow. (The Blalock shunt present, although patent, was exceedingly small.)

We believe that the patient's postoperative course and death were due to the inability of the nonatrialized portion of the left ventricle to cope with the sudden increase in work load occasioned by closure of the ventricular septal defect and resection of the pulmonary stenosis. Recognition of a left Ebstein's anomaly, therefore, becomes of paramount importance to the surgeon.

The preoperative diagnosis of left Ebstein's anomaly poses great difficulties, especially in the absence of clinical evidence of incompetence of the left atrioventricular valve or left atrial enlargement. Perhaps, with increasing knowledge, selective angiocardiography and left heart catheterization will prove helpful. It may be stated, however, that anomalies of the left atrioventricular valve in association with corrected transposition of the great vessels are sufficiently common to warrant digital exploration of the left atrium in all cases of corrected transposition subjected to intracardiac operative procedures.

Summary

A case of left Ebstein's anomaly in association with corrected transposition of the great vessels, subpulmonary stenosis and a ventricular septal defect is presented. Surgical treatment of the subpulmonary stenosis and ventricular septal defect was carried out on cardiopulmonary bypass. The anatomic handicaps peculiar to corrected transposition which confront the surgeon in correcting these associated anomalies are discussed. The left Ebstein's anomaly discovered at autopsy was unsuspected during life and could not be recognized by external examination of the heart in this case. At postmortem examination the nonatrialized portion of the left ventricle appeared too small to maintain the systemic circulation. It is believed that this factor alone led to the patient's death once the ventricular septal defect had been closed.

Attention is again drawn to the common occurrence of abnormalities of the left atrioventricular valve in association with corrected transposition, left Ebstein's malformation being one of the rarer forms. It is recommended that digital exploration of the left atrium be carried out in all cases of corrected transposition selected for open cardiotomy procedures.

Acknowledgment

We are indebted to Mr. Gerard Schölle and the Department of Medical Illustrations, Albany Veterans Administration Hospital, for the illustrations.

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Primary and Secondary Dextrocardia

Their Differentiation and the Role of Cineangiocardiography in Diagnosing Associated Congenital Cardiac Defects*

JOHN S. HANSON, M.D. *and* BURTON S. TABAKIN, M.D.

Burlington, Vermont

ALTHOUGH FOR centuries the phenomenon of dextrocardia was considered primarily a medical curiosity, modern cardiac surgery and diagnostic technics have placed these rotational anomalies in a new light. Today it does not suffice merely to diagnose the presence of the heart in the right thorax by auscultation and routine radiography. Differentiation must be made between true "primary" dextrocardia which is always congenital and "secondary" dextrocardia which may be either acquired or congenital. Furthermore, the technics of cardiac catheterization and selective angiocardiography afford more exact information as to the existence of associated intracardiac defects and the feasibility of their repair. Mandelstamm and Reinberg[1] presented a classification of primary dextrocardias in 1928 to which little has been added. In brief, this defines three possible variations of the "right-sided heart" as follows:

1. *Dextrocardia with total or partial situs inversus.* In well over 90 per cent of such cases there is no associated intracardiac defect and a true "mirror image" of normal cardiac position exists. This inversion of the cardiac chambers is such that the normal anterior position of the right atrium and right ventricle is preserved (Fig. 1B). As a consequence of the inversion of the relationships in the frontal plane, the venae cavae assume a position to the left of the spine, the pulmonary veins entering to the right. The aorta lies to the right of the spine but maintains its position posterior to the pulmonary artery which originates to the left.

In those cases of situs inversus and dextrocardia complicated by congenital cardiac defects, the latter are usually of complex nature involving absence of septa, valvular atresia and chamber hypoplasia.

2. *Isolated dextrocardia (without situs inversus) with chamber inversion.* Although existence of this anomaly was predicted in the original classification, Keith[2] has raised considerable doubt that such a variation of dextrocardia exists, either with a normal or malformed heart. Previous reports of such cases[3–6] are questionable in the accuracy of their anatomic details, and it is presently in the realm of conjecture whether a true, isolated, mirror-image dextrocardia can exist in the absence of other organ heterotaxy.

3. *Isolated dextrocardia without inversion of chamber.* This final type is the most common and, in contradistinction to dextrocardia associated with situs inversus, almost always has concomitant intracardiac anomalies. Since no true chamber inversion is involved here, the cardiac cavities assume the relationships illustrated in Figure 1C. The left atrium and ventricle occupy anterior positions, the right atrium and ventricle lying posteriorly. The aorta maintains its normal left-sided course and relation to the pulmonary artery. Likewise, the venae cavae course to the right of the spine. Various minor rotational differences from this general pattern may be encountered.

Cyanosis is usually a dominant feature of such dextrocardia, being absent in less than 20 per cent of cases. Those associated primary defects most often encountered are stenosis of the tricuspid valve or atresia (with or without other valvular stenosis or atresia and vessel transposition), single ventricle, transposition of the great vessels, Fallot's tetralogy and atrioventricularis communis. It should be noted that complete or corrected transposition of the

* From the Cardiopulmonary Laboratory, University of Vermont College of Medicine, Mary Fletcher Hospital, Burlington, Vermont.

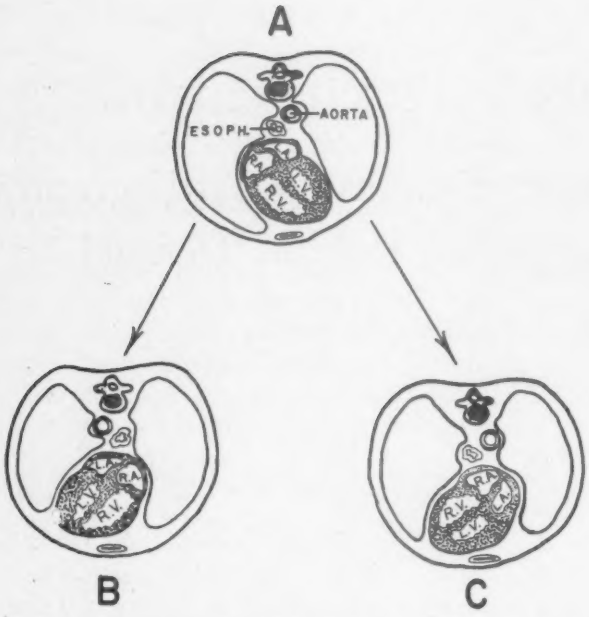

FIG. 1. A, normal cardiac relationships. B, true "mirror image" dextrocardia with inversion of atrial positions. C, "isolated" dextrocardia; normal atrial interrelations.

great vessels is present in about 75 per cent of such cyanotic dextrocardias. Less serious associated cardiac anomalies include partial abnormal venous return and aberrant venae cavae.

In view of this, it is a relatively simple and accurate process to clinically characterize a given case of primary dextrocardia. With associated total or partial situs inversus, the chances are great that the heart is normal. If, however, symptoms or clinical findings are indicative of a cardiac defect and there is no cyanosis, the anomaly is probably relatively simple (atrial septal defect, ventricular septal defect or anomalous venous drainage). In the presence of cyanosis more complicated defects are to be expected.

In the great majority of cases, however, *isolated* dextrocardia implies any one or combination of several complicated cardiac abnormalities, especially in that large majority of cases which is cyanotic. Most commonly encountered here will be tricuspid atresia and transposition of the great vessels, usually with other associated defects.

Configuration of the electrocardiogram can, with only one exception, no longer be regarded as providing irrefutable evidence for or against the various forms of dextrocardia. Only in situs inversus without cardiac defects is the classic pattern of P wave inversion with

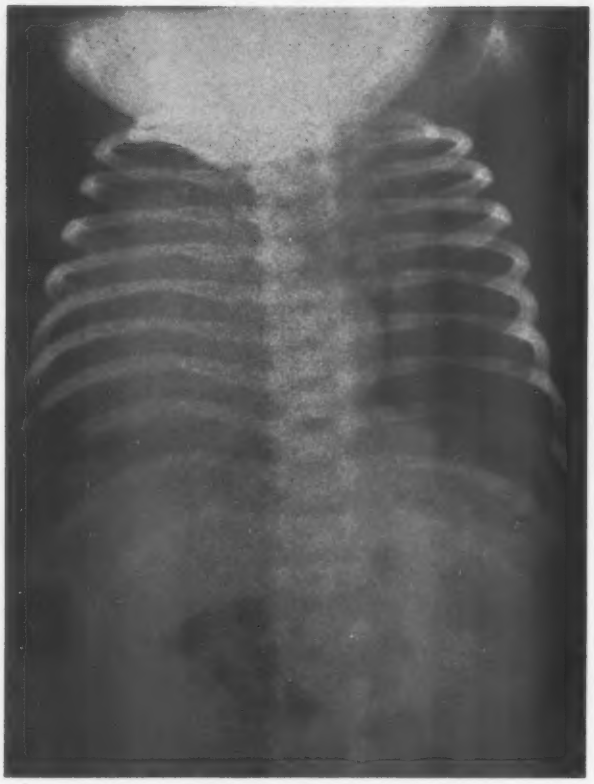

FIG. 2. Case 1. Posteroanterior radiograph demonstrating dextrocardia of the "isolated" variety.

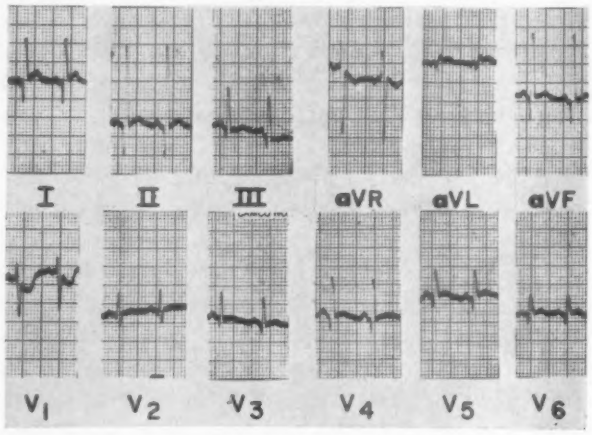

FIG. 3. Case 1. Electrocardiogram. Note the upright P waves, suggesting normal frontal relationship of the atria.

interchanging of leads II and III universally seen. "Complicated situs,"[7] as well as the usual complicated isolated dextrocardia without situs, are both associated with widely varying electrocardiographic patterns. True atrial inversion may exist in the face of upright P waves in lead I and, conversely, negative P waves may be seen without atrial inversion. Keith[2] reports moment-to-moment changes in P wave configuration. In the presence of grossly dis-

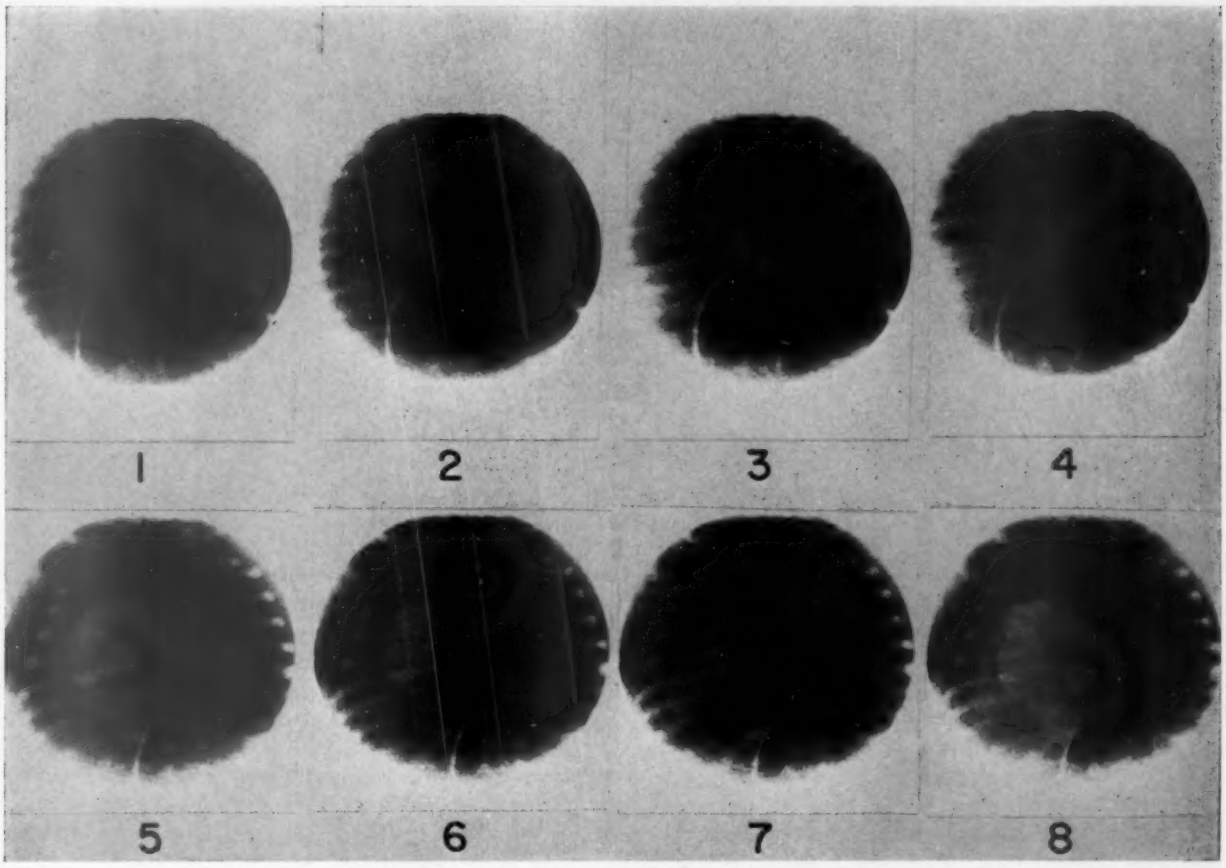

FIG. 4. Case 1. Representative cinefluoroscopic frames from selective angiocardiography. The first four pictures show contrast medium injection in the left atrium from a PA projection. 1, filling of left atrium. 2, filling of left ventricle. 3, filling of aorta. 4, filling of right pulmonary artery via patent ductus. Second series of four pictures show dye injection in right atrium and posteroanterior projection. 5, filling of right atrium. 6, filling of left atrium through an atrial septal defect, absence of right ventricular filling. 7, filling of left ventricle. 8, filling of aorta.

torted cardiac anatomy, the electrocardiogram may be of little or no value.

Therefore, precise diagnosis of the existing congenital cardiac defects will rest most heavily on radiological technics. A gastrointestinal x-ray series will allow definition of a situs inversus. Roentgenograms of the chest showing mediastinal masses, primary pulmonary disease, atelectasis and lung agenesis, will give helpful information in deciding whether the position of the heart in the right hemithorax is secondary to one of these factors or truly a primary anomaly. Finally, selective cineangiocardiography will usually provide the ultimate delineation of position of the chambers and structural irregularities. The following case reports illustrate the sequence of diagnostic reasoning and investigation applied to two infants with dextrocardia recently seen in our center.

CASE REPORTS

CASE 1. *Isolated Dextrocardia Without Chamber Inversion Associated With Multiple Congenital Defects:* T. M., an eighteen day old white male infant, was admitted to the Mary Fletcher Hospital from a neighboring hospital for evaluation of suspected congenital heart disease. In the immediate postpartum period it was noticed that the patient had frequent episodes of severe cyanosis, especially during feeding. Apnea with even more intense cyanosis occurred several times daily. The baby was place in an incubator and transferred to a neighboring hospital. There routine roentgenograms demonstrated dextrocardia (Fig. 2) with a grossly enlarged cardiac shadow. A marked increase in pulmonary vasculature, indicative of a left to right shunt, was also noted. The gastric fundus, liver, and spleen were seen in their normal positions. No pulmonary, mediastinal or diaphragmatic abnormalities were detected which would account for the dextrocardia. An electrocardiogram showed a normal sinus tachycardia with upright P waves in lead I (Fig. 3) and predominantly left ventricular preponderance. It was believed that the Q wave changes in leads I to III and V_4-V_6 with concomitant S-T elevation might represent a lateral wall infarction as sometimes appears in aberrant origin of the left coronary artery.

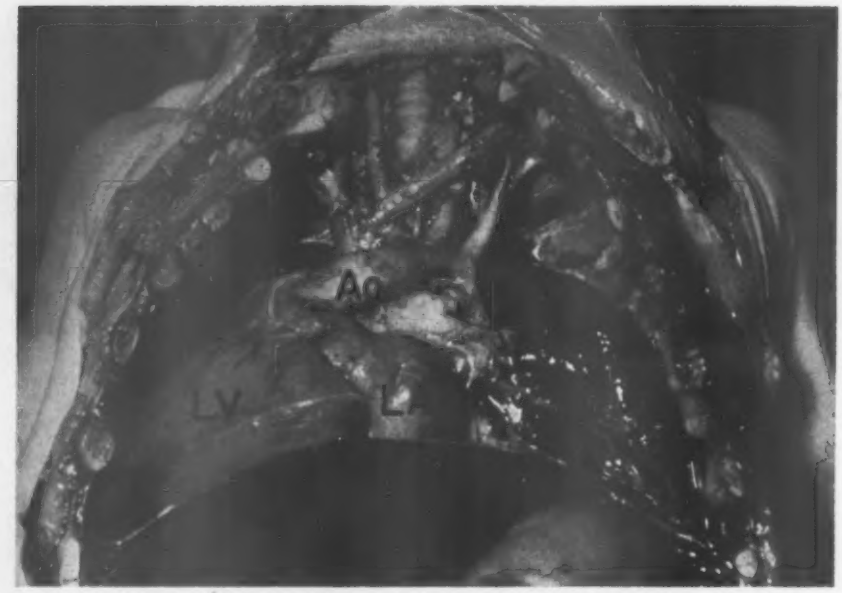

FIG. 5. Case 1. Autopsy specimen showing the heart and lungs *in situ*. LV = left ventricle; LA = left atrium; Ao = aorta.

Physical examination revealed a pulse of 166 per minute and respirations of 60. The blood pressure in both arms and the right leg was 70 mm. Hg systolic. The lungs were clear and resonant. The point of maximal cardiac impulse was diffusely distributed at the third and fourth right intercostal spaces near the anterior axillary line. A grade 3 holosystolic murmur was auscultated over the entire precordium. The second sound in the second right interspace was markedly accentuated. Femoral pulses were easily palpable bilaterally. Hemoglobin was 20.4 gm. per 100 ml., hematocrit 59 per cent, white blood cell count of 14,850 with a normal differential count. Urinalysis was within normal limits.

Following these studies, the patient was transferred to this facility for cardiac catheterization and angiocardiography. Physical findings and laboratory data were unchanged following admission.

Precatheterization evaluation followed the lines of reasoning as has been outlined: without evidence for an associated situs inversus, the dextrocardia was thought in all probability to represent an isolated phenomenon. The high incidence of complex cardiac malformations in this situation, coupled with the patient's severe cyanosis and cardiomegaly and increased pulmonary vascular markings, were strong indications that we were dealing with a complicated problem. The electrocardiogram suggested that chamber inversion was not involved, and the left ventricular predominance was thought consistent with hypoplasia of the right ventricle. The entire picture was consistent with tricuspid atresia and associated atrial septal defect, as well as a left to right shunt at the ventricular and/or ductus level. Since it was believed that precise diagnosis might allow consideration of palliative surgery, the following procedures were undertaken.

Catheterization and Cineangiocardiographic Findings: Under local anesthesia with 100 per cent O_2 inhalation, cardiac catheterization was carried out via the right saphenous vein. It was possible to advance the catheter tip into the superior vena cava which lay on the right. In addition, both right and left atria were entered, as well as a pulmonary vein from the left atrium. Blood oxygen saturations from these positions indicated a right to left shunt at the atrial level, although pulmonary vein blood was only 92 per cent saturated. Despite continued attempts to enter a ventricular cavity, this was not accomplished.

After insertion of a multiple side-holed angiocardiography catheter, dye contrast studies were carried out from two positions. Using 5 cc. of Hypaque®-M 90% medium for each injection, cinefluorograms were recorded through the Philips five inch image intensifier at film speed of 64 frames per second. Representative frames of the studies are presented in Figure 4. The studies confirmed the diagnosis of tricuspid atresia, interatrial septal defect and right to left flow, very small or absent right ventricle and patent ductus arteriosus.

During the following twenty hours the infant continued to have frequent periods of intense cyanosis and apnea. Although a vena cava-left atrial anastomosis was considered, it was impossible to carry out any form of anesthesia without producing stridor and periods of apnea with increased cyanosis. The patient died suddenly on the morning after catheterization.

Autopsy Findings: The heart was grossly enlarged (Fig. 5), weighing with the lungs 90 gm. (normal mean for this age is 65 gm.). Isolated dextrocardia without inversion of the chambers was seen. Agenesis of the tricuspid valve was associated with marked right ventricular hypoplasia. That portion of the

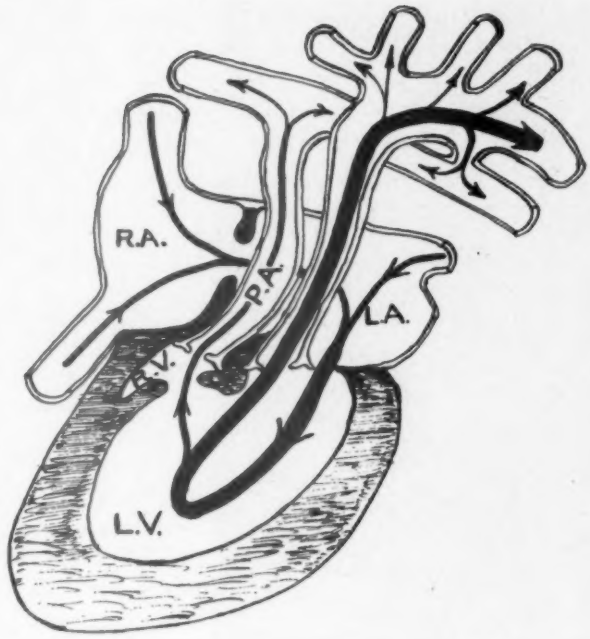

FIG. 6. Case 1. Diagrammatic representation of congenital cardiac defects and circulatory pathways. RA = right atrium; RV = right ventricle; LA = left atrium; LV = left ventricle; PA = main pulmonary artery.

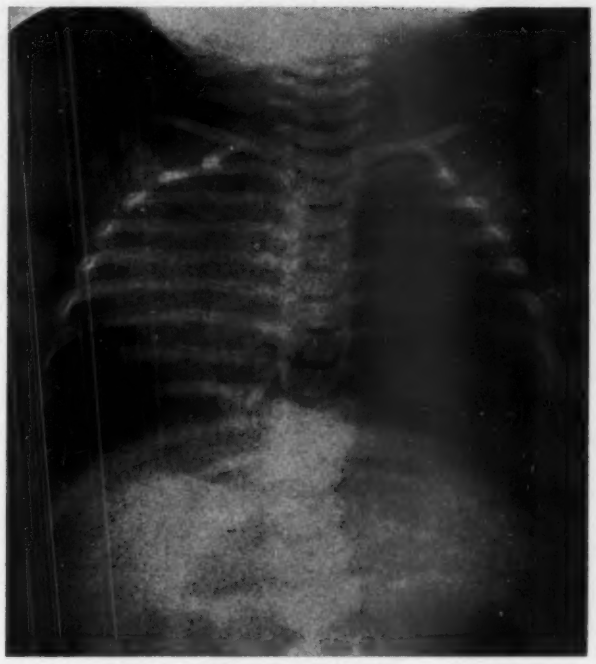

FIG. 7. Case 2. X-ray film of the chest. Note the "pushed-up" appearance of the cardiac shadow in contrast to Figure 2.

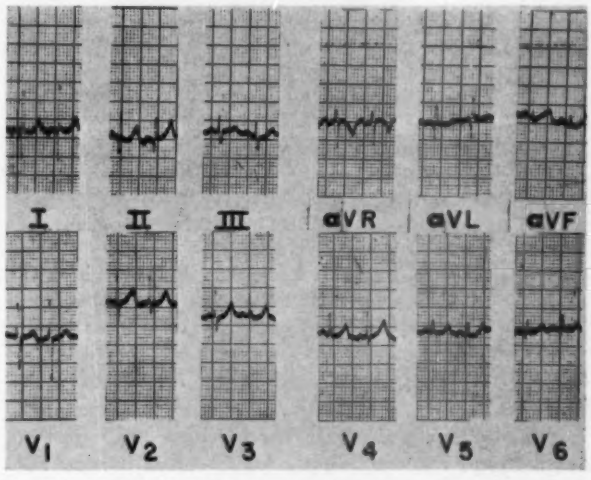

FIG. 8. Case 2. Electrocardiogram. The P waves show consistent diphasic configuration in lead I, the initial and major component being negative.

right ventricle which was identifiable communicated with the markedly hypertrophied left ventricle through a small membranous ventricular septal defect. The pulmonary valve was within normal limits and opened into a normal-sized main pulmonary artery which was, however, situated to the left and posterior to the aorta, representing a "corrected" transposition of the great vessels. A large, 1.5 cm. atrial septal defect and a patent ductus arteriosus were also demonstrated. Coarctation of the aorta distal to the origin of the left subclavian artery was present. The existing anatomic relationships and blood flow are illustrated in Figure 6.

CASE 2. *Secondary Dextrocardia Due to Congenital Agenesis of Right Lung:* C. A., a six month old white female infant, was transferred to this hospital from another city for evaluation of a "mass in the upper lobe of the right lung" and "collapse of the upper lobe of the right lung." Although the child had been noted by the parents to have rapid respirations since birth, she had apparently been entirely well until two weeks prior to admission here when an infection of the upper respiratory tract with wheezing developed. Improvement did not follow penicillin therapy by her family physician, and the child was admitted to her local hospital. X-ray films taken at that time were interpreted as showing collapse of the upper lobe of the right lung and a large mass in the right hemithorax, possibly the heart.

Past history was unremarkable. The patient was one of twins, the sibling being supposedly healthy in every respect. Growth and development were within normal limits and the parents had never noticed cyanosis.

Physical examination on admission revealed a chubby, healthy-looking baby with good skin color. Respirations were 48 per minute, but other vital signs were within normal limits. Breath sounds were audible over both hemithoraces both anteriorly and posteriorly without adventitious sounds. Heart sounds were definitely more prominent over the right anterior side of the chest. Some observers heard a grade 2-3, short systolic murmur along the left sternal border. The point of maximal cardiac impulse was in the fourth right intercostal space in the midclavicu-

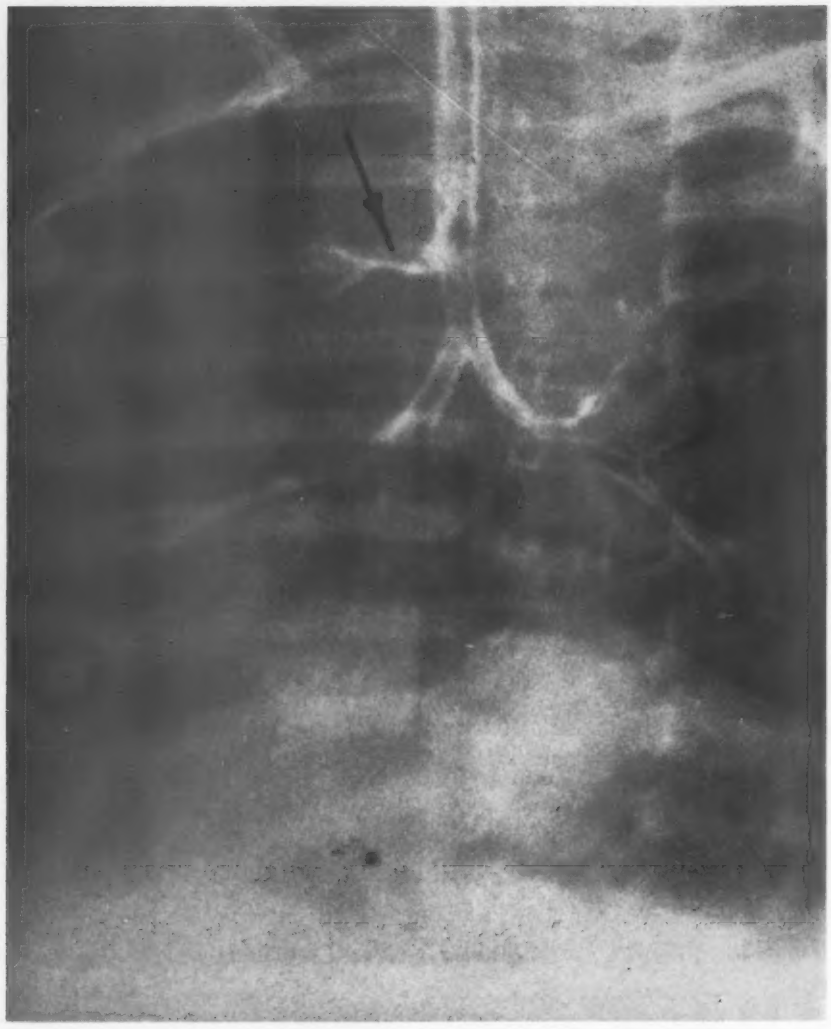

FIG. 9. Case 2. Representative bronchogram. Atretic stump of right main bronchus is indicated by arrow.

lar line. The liver was palpable 2 fingerbreadths below the right costal margin.

X-ray examination with fluoroscopy and barium instillation in the esophagus showed very slight displacement of the trachea to the right. The cardiac shadow was seen in the right hemithorax (Fig. 7). Pulmonary vasculature was thought to be prominent and the radiologist's impression was that there might very possibly be atelectasis of the upper lobe of the right lung. Stomach and small bowel were seen in their normal positions, but no spleen shadow could be detected.

Electrocardiogram (Fig. 8) showed inverted and diphasic P waves in leads I and aVR, but was otherwise unremarkable except for decreased potentials in the left chest leads.

Two days following admission *bronchography* was carried out to evaluate bronchial distribution and lung position. As seen in Figure 9, total absence of the right bronchial tree was noted, the left lung having herniated into the right hemithorax pushing the heart with it. Because of reluctance on the part of the patient's parents, cardiac catheterization and angiocardiography were not carried out. *Final diagnosis* was congenital agenesis of the right lung with resultant overexpansion of the left lung and displacement of the heart to the right side of the chest.

COMMENTS

Differentiation of primary and secondary dextrocardia should not present any great diagnostic problems. The unexpected finding of dextrocardia with associated partial or total situs inversus in a healthy subject is a true primary dextrocardia, and in the vast majority of cases of no medical importance. As in Case 1 reported, the presence of cyanosis, a loud cardiac murmur and displacement of only the heart should strongly suggest primary dextrocardia of the isolated type with serious associated cardiac defects. An apparently healthy subject

with dextrocardia unaccompanied by situs inversus or thoracic deformity, as exemplified by Case 2, may be difficult to categorize initially.

Although the opinion is still generally held that the electrocardiogram will provide an exact differentiation of dextrocardia,[8] such is apparently not entirely true. Case 2 illustrates the diagnostic fallacy of automatically associating P wave negativity with primary dextrocardia involving atrial inversion. Such P wave abnormality might also be seen in isolated dextrocardia unassociated with atrial inversion but with other cardiac malformations. Conversely, the lack of P wave inversion in the face of true atrial inversion has already been mentioned.

Realizing that electrocardiographic information cannot provide the final word in differentiating the various types of dextrocardia, heavy reliance must be placed on specialized radiographic technics. To distinguish between primary and secondary dextrocardia, anomalies of the lung, tumors, diaphragmatic malformations and mediastinal displacements must be looked for by the technics of bronchography, tomography, angiography and contrast study of the gastrointestinal tract. The almost innumerable variety of structural malformations occurring with primary dextrocardia necessitates employment of cardiac catheterization and selective angiocardiography for definition.

Summary

Two cases are presented to illustrate the differential diagnosis of primary and secondary dextrocardia. As an example of the former, Case 1 demonstrated features of isolated dextrocardia without heterotaxy of other organs. Investigation revealed serious intracardiac malformations usually seen in such cases, consisting in this instance of tricuspid, atrial and ventricular septal defects, corrected transposition of the great vessels and patent ductus arteriosus. By way of contrast, Case 2 represents secondary dextrocardia as a result of congenital agenesis of the left lung. Diagnosis in this instance was established by use of bronchography. The necessity of employing a variety of radiographic technics for differentiation of primary and secondary dextrocardia is stressed, and the value of cineangiocardiography in delineating associated congenital cardiac defects is demonstrated.

Acknowledgment

We are very grateful to Drs. Borys Surawicz and Donald B. Miller who kindly referred Cases 1 and 2, respectively. For the interpretation of the electrocardiogram in Case 1 we wish to thank Dr. Eugene Lepeschkin.

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Increased Bronchial Collateral Circulation in a Patient with Transposition of the Great Vessels and Pulmonary Hypertension*

ROLAND FOLSE, M.D., WILLIAM C. ROBERTS, M.D. *and* WILLIAM P. CORNELL, M.D.

Bethesda, Maryland

IT IS WELL established that patients with cyanotic congenital heart disease characterized by diminished pulmonary blood flow have increased collateral circulation to the lungs through enlarged bronchial arteries. The incidence, stimuli for development and structural arrangement of these collateral vessels are not well understood.

Large bronchial vessels are commonly found in patients with stenotic lesions in the right side of the heart or the pulmonary artery producing an intracardiac right to left shunt such as is seen in tetralogy of Fallot, pulmonic stenosis with atrial septal defect or tricuspid atresia. In these patients the pulmonary artery pressure and blood flow are diminished. Intravascular thromboses in the pulmonary vascular bed, presumably secondary to capillary stasis and polycythemia, may further diminish the pulmonary blood flow and thus further the need for bronchial collaterals.[1] Likewise, in patients with complete absence or atresia of the pulmonary arteries, communications arising directly from the aorta persist from fetal life and are essential not only for the nourishment of the pulmonary structures but also for supplying the lungs with desaturated blood in order to provide for exchange of gases.[2]

Bronchial collaterals may also develop in acyanotic patients. For example, the congenital absence of one main pulmonary artery is associated with enlarged bronchial arteries to that lung.[3] In other diseases, additional mechanisms may lead to increased collateral circulation to the lungs. Patients without heart disease, such as those with pulmonary infarction, bronchiectasis, tuberculosis, emphysema or lung tumors, may have increased bronchial blood flow to the diseased portions of the lungs.

It has not been generally appreciated that patients with cyanotic congenital heart disease and pulmonary hypertension may also have extensive collateral circulation to the lungs. This communication describes an infant with complete transposition of the great vessels, a ventricular septal defect and pulmonary hypertension, who also had markedly increased pulmonary collateral blood flow.

CLINICAL SUMMARY

T. N., a fourteen month old male infant, had been cyanotic since birth. His early growth and development were somewhat retarded and he had frequent respiratory infections but no episodes of severe cyanosis or squatting. He was described as being an active child with some limitation due to fatigability. There was no history of heart failure.

On examination the patient was moderately cyanotic at rest and had evidence of clubbing of the digits. He was somewhat small for his age, his weight being in the tenth percentile on the anthropometric chart. The heart was enlarged to both the right and left sides of the sternum. There was a lift over the lower left sternal area, but no thrill was palpable. The second sound at the base was slightly accentuated and was thought to be single. There was a soft, grade 1–6 early systolic murmur heard along the lower left sternal border. The hematocrit was 75 per cent and the hemoglobin 21.5 gm. per 100 ml. The electrocardiogram demonstrated right atrial enlargement, right axis deviation and right ventricular hypertrophy (Fig. 1). Cardiac fluoroscopy revealed enlargement of both ventricles with narrowing of the base of the heart. The horizontal course of tortuous vessels in the hilar regions suggested the presence of prominent bronchial arteries.

At catheterization the pulmonary artery was not

* From the Clinic of Surgery, National Heart Institute and Department of Pathologic Anatomy, the Clinical Center, National Institutes of Health, Bethesda, Maryland.

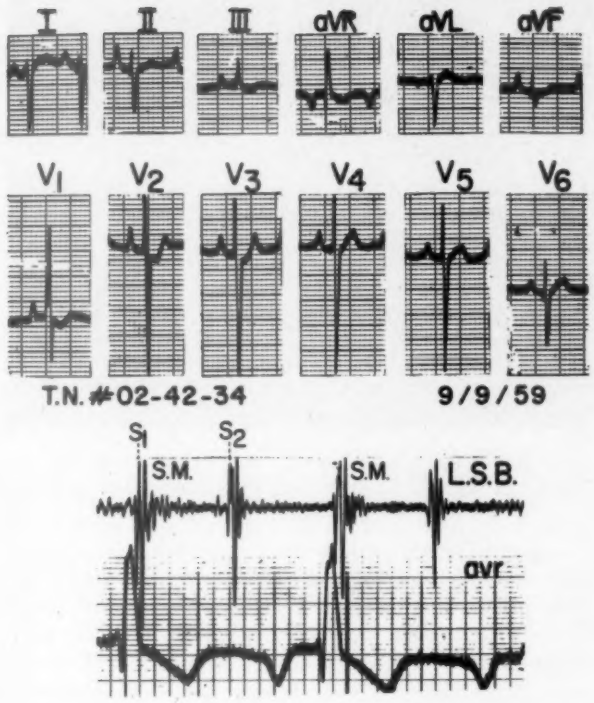
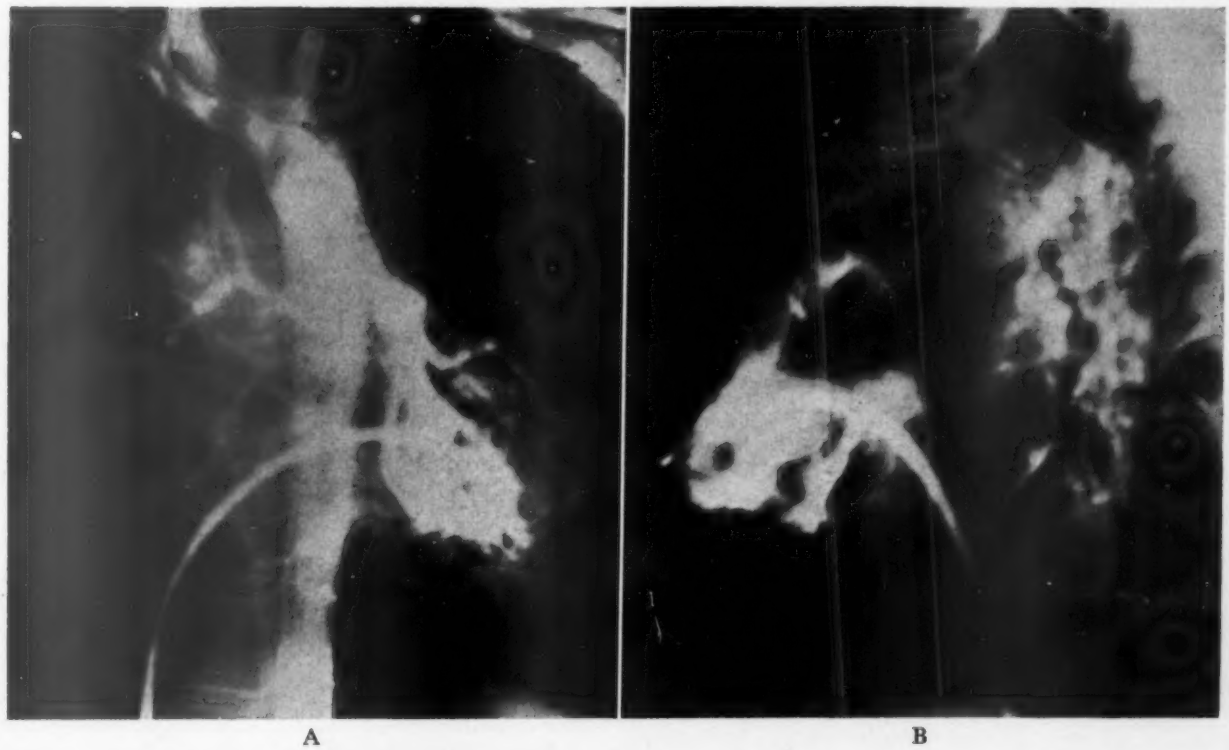


FIG. 1. Electrocardiogram and phonocardiogram. S.M. = systolic murmur; L.S.B. = left sternal border.

entered. The systemic arterial oxygen saturation was 43 per cent under general anesthesia. *A selective right ventricular angiocardiogram* (Fig. 2) was performed which demonstrated that the aorta arose from the anatomic right ventricle. The left ventricle and pulmonary artery were not opacified in the early films. Large bronchial arteries were seen to arise from the descending aorta and appeared to be equally distributed to all parts of both lungs. The right main pulmonary artery visualized well in the later films, suggesting that it was filled by communications with the bronchial arteries. Because of the lack of prominent pulmonary vascularity on the roentgenogram of the chest and the presence of extremely prominent collateral vessels, it was believed that the patient had complete transposition of the great vessels with associated pulmonic stenosis and would, therefore, benefit from a subclavian-pulmonary artery anastomosis.

At operation the pulmonary artery, which was approximately the same size as the aorta, was observed to arise from the left ventricle and in a position directly posterior to the aorta. Pressures measured simultaneously in the pulmonary artery and aorta were equal. A large number of dilated bronchial arteries and veins were present in the hili of the lungs, in the interlobar fissures and along the subpleural surface of the lungs. Because of the high pressure in the pulmonary artery, an anastomosis was not performed. Postoperatively, the patient became



A B

FIG. 2. Selective right ventricular angiocardiogram demonstrating complete transposition of the great vessels and large bronchial arteries arising from the descending thoracic aorta. A, posteroanterior view; B, lateral view.

FIG. 3. The right ventricle, aortic valve and aorta are opened. The aorta lies anteriorly and arises exclusively from the right ventricle. The coronary arteries arise from the aorta (narrow white pointers). A ventricular septal defect (thick white arrow) is located immediately inferior to the supraventricular muscle. Note the large size of the coronary arteries.

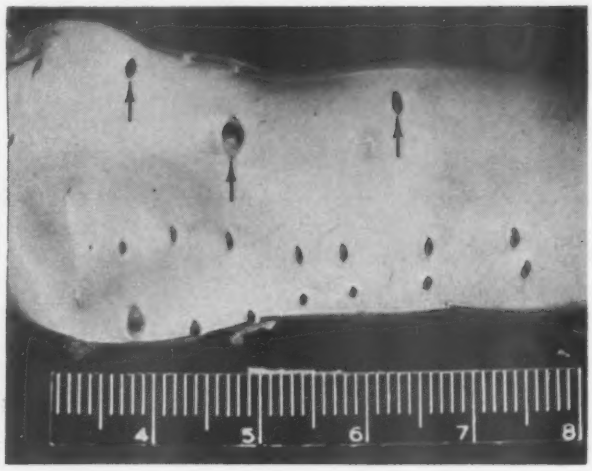


FIG. 4. Descending thoracic aorta demonstrating the markedly dilated ostia (arrows) of the bronchial arteries.

progressively more cyanotic, and his condition gradually deteriorated until he died eighteen hours after operation.

PATHOLOGIC FINDINGS

Necropsy confirmed the operative finding of complete transposition of the great vessels. The aorta arose exclusively from the right ventricle (Fig. 3) and the pulmonary trunk from the left ventricle. The ascending aorta lay directly anterior to the pulmonary trunk. Both ventricles were hypertrophied; the left measured 0.1 cm. and the right, 0.9 cm. in greatest thickness. A ventricular septal defect was present immediately inferior to the supraventricularis muscle (Fig. 3). Both atria were dilated, the right more than the left. The atrial appendages were normally situated. A valvular-competent foramen ovale was present. The venae cavae entered the right atrium, and the pulmonary veins entered the left atrium in a normal manner. The atrioventricular valves were normally developed. The pulmonic valve lay posteriorly and joined the anterior mitral leaflet in a manner similar to the connections between the mitral and aortic valves in a normal heart. The cusps of the pulmonic and aortic valves were delicate and pliable and there was no evidence of stenosis. Three large bronchial arteries arose directly from the descending thoracic aorta (Fig. 4) and coursed along the posterior aspect of the lower trachea and main bronchi before entering the hili of the lungs (Fig. 5). No atherosclerotic changes were present in the pulmonary artery or aorta. The ostia of the coronary arteries arose from the two posterior sinuses of Valsalva (Fig. 3).

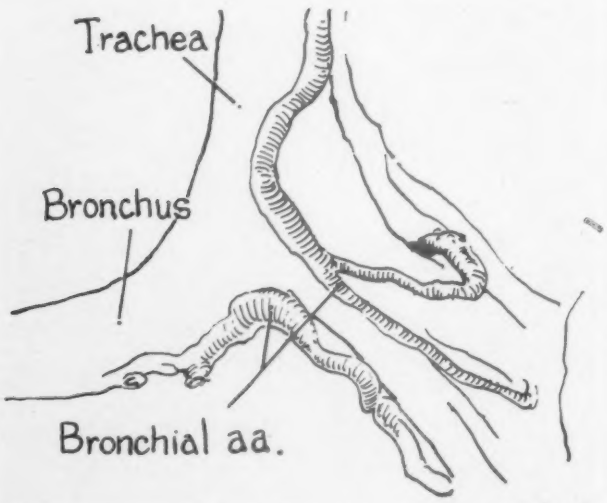
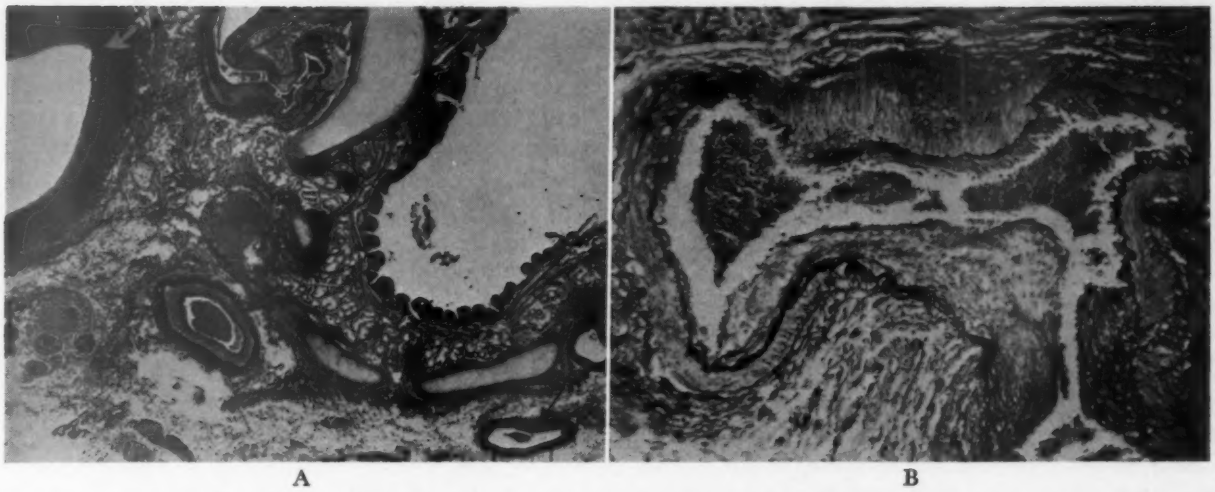


FIG. 5. Diagram (traced from the original photograph of this area) illustrating the large bronchial arteries coursing along the posterior aspect of the lower trachea and main bronchi before entering the hili of the lungs.

Microscopically, in the sections from the hili of the lungs many dilated, thick-walled bronchial arteries surrounding the bronchi were seen (Fig. 6A). Also, there was proliferation of the intima of some bronchial arteries (Fig. 6B), a finding which has not received attention in the past. Many dilated bronchial veins were seen in the subpleural areas of the lungs, particularly the hilar regions. Sections from the main pulmonary arteries showed the elastic fibers arranged in an orderly fashion similar to those found in a fetal pulmonary artery (Fig. 7). This picture is noted in the lungs of patients in whom pulmonary hypertension has been present from birth and in whom the normal transition to the adult type of pulmonary artery has not taken place.[4] The elastic and muscular pulmonary arteries were dilated, and the latter showed medial hypertrophy and occasional intimal thickening. The lumina of the pulmonary arterioles were narrowed by intimal proliferation (Fig. 8).



A B

FIG. 6. A, photomicrograph of lung in hilar region demonstrating thick-walled, dilated bronchial arteries (black arrows) surrounding a bronchus. There is intimal thickening in addition to medial hypertrophy of the bronchial artery in the uppermost portion of the figure. A large elastic pulmonary artery (white arrow) of the fetal type is present in the left upper corner of the figure. (Elastic van Giesson stain, original magnification × 17.) B, close-up view of the large bronchial artery appearing in A. Note the marked intimal proliferation and medial hypertrophy. (Elastic van Giesson stain, original magnification × 120.)

COMMENTS

It was demonstrated early in experiments on dogs by Mathes and associates[5] that bronchial collateral circulation to the lungs will develop following obstruction of the pulmonary artery. Liebow et al.[6] have traced the pathway of development of collateral vessels from the bronchial artery to the pulmonary artery to the pulmonary capillaries, with drainage directly into the pulmonary veins or into the azygos system by way of the bronchial veins.

There are few documented reports in the literature of augmentation of the bronchial circulation in association with transposition of the great vessels. The combination of complete transposition of the great vessels with pulmonary hypertension and enlarged bronchial arteries in particular, has not been well described previously. The case of transposition of the great vessels which Cockle[7] described in 1863 had enlarged bronchial vessels and probably a normal or increased pulmonary artery pressure, since there was no stenosis of the pulmonic valve and the pulmonary artery was larger than the aorta. Also, no obstruction of the pulmonary valve was noted in pathologic findings of the patient with complete transposition in whom Cudkowicz et al.[8] demonstrated extensive bron-

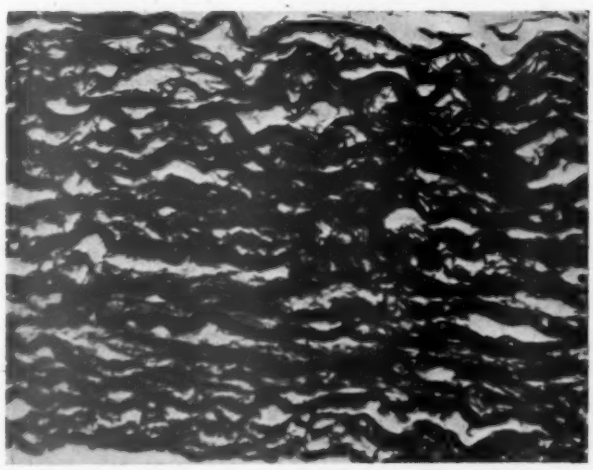


FIG. 7. Photomicrograph of main pulmonary artery demonstrating the aorta-like fetal configuration of the elastic lamellae. (Elastic van Giesson stain, original magnification × 450.)

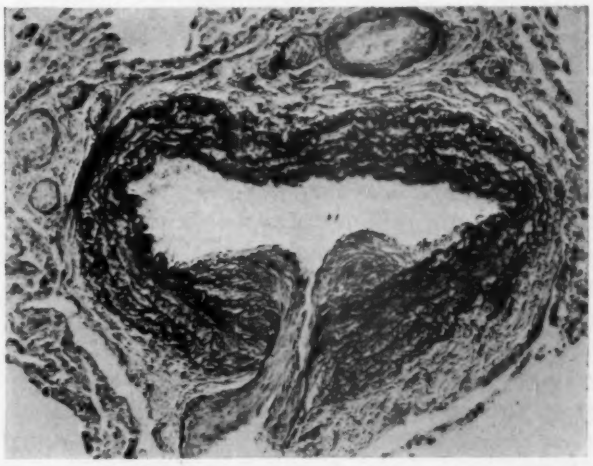


FIG. 8. Photomicrograph of pulmonary artery demonstrating marked intimal proliferation and narrowing at the junction of an arteriolar branch. (Elastic van Giesson stain, original magnification × 155.)

chial collateral circulation by injection technics. The pulmonary arteries were dilated and communicated freely with the vasa vasorum supplied by the bronchial arteries.

Bronchopulmonary arterial communications may be found in patients with single ventricle and pulmonary hypertension as in the case reported by Heath,[9] in which bronchial collaterals were prominent in the adventitia of large arteries, surrounding the bronchi and along the visceral pleura. In a similar case illustrated by Liebow,[10] proliferated bronchial arteries were demonstrated to communicate with tortuous pulmonary vessels. In the lungs of patients with Eisenmenger's complex, collateral channels in the form of angiomatoid lesions may connect the pulmonary and bronchial circulations.[11] Similar lesions have been reported in patients with patent ductus arteriosus with pulmonary hypertension[12,13] and in those with atrial septal defect and pulmonary hypertension;[14] these vessels may divert blood to the alveolar capillaries.

It appears, therefore, that there is a wide spectrum of malformations in which collateral channels to the lungs may develop. The presence of reduced pulmonary blood flow or the absence of elevated pulmonary vascular resistance should not be suspected in a patient with cyanotic congenital heart disease merely because of the existence of enlarged bronchial vessels. Catheterization of the pulmonary artery is difficult or impossible in patients with transposition of the great vessels, single ventricle, truncus arteriosus and other complicated forms of cyanotic heart disease; therefore, the use of right- and left-sided angiocardiography would be valuable in assessing the size of the pulmonary artery, the relative amount of pulmonary blood flow and in estimating the pulmonary artery pressure.

In the patient reported herein a right ventricular angiocardiogram was performed, but because of the presence of complete transposition of the great vessels only the aorta was opacified; the pulmonary artery could not be visualized. As this case illustrates, the clinical picture associated with cyanotic heart disease and pulmonary hypertension may be confused with that associated with obstruction to pulmonary flow secondary to obstruction in the right ventricular outflow tract or at the pulmonary valve. The reduced pulmonary vascularity on the roentgenogram in this patient was suggestive of a reduced pulmonary artery pressure. The closely split second heart sound heard at the base resulted from the presence of equal pressures in the great vessels rather than from an obstruction to right ventricular outflow. The very soft systolic murmur probably indicated that only a small amount of blood passed across the ventricular septal defect, due to the equal ventricular pressures. Accordingly, it is essential that a thorough angiographic and hemodynamic evaluation of the pulmonary vascular bed precede any operative procedure designed to increase pulmonary blood flow in patients with transposition of the great vessels.

Summary

The clinical, diagnostic and pathologic findings in a fourteen month old infant with complete transposition of the great vessels, ventricular septal defect and pulmonary hypertension with increased bronchial collateral circulation are presented. It is emphasized that the presence of increased bronchial collateral blood flow is not necessarily associated with decreased pulmonary blood flow due to obstruction to right ventricular outflow, but may also be associated with pulmonary hypertension and elevation of pulmonary vascular resistance. Thus, the presence of enlarged bronchial vessels should not indicate that the patient will benefit from an operation designed to increase the pulmonary blood flow. The importance of right and left ventricular angiocardiograms in the preoperative assessment of the pulmonary vascular bed is discussed.

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Congenital Corrected Transposition of the Great Vessels with Situs Inversus and Dextrocardia

Report of Surgical Repair of Associated Defects in a Patient with Pulmonary Stenosis, Interatrial Communication and Persistent "Left" Superior Vena Cava*

W. Spencer Payne, M.D., F. Henry Ellis, Jr., M.D. *and* James C. Hunt, M.D.

Rochester, Minnesota

Reports of successful operations on patients with congenital corrected transposition of the great vessels are few.[1,2] The anomaly itself is uncommon, and in association with situs inversus it is a rarity. In addition to the present case† Schiebler and associates[2] reported only one other case of associated situs inversus in a series of thirty-three patients with corrected transposition. The patient showed isolated levocardia. Espino-Vela and co-workers[3] reported one case with associated situs inversus and dextrocardia. In the case described by Platzer[4] the patient had situs inversus with levocardia.

The present case is of interest not only because of the rarity of the condition in situs inversus and the attendant difficulties of surgical orientation but also because of the unusual combination of defects which permitted successful surgical repair.

Case Report

A thirty-one year old unmarried white male bookkeeper had had a heart murmur and mild cyanosis since birth. His chief symptoms were moderate dyspnea and palpitations on exertion. Growth and development were within normal limits and, although limitation was not great, he had lived a sedentary existence. His alleged identical twin was considered normal. He had no other known defects except a supernumerary digit which had been amputated. At twenty-three years of age the patient had experienced a febrile illness of several weeks' duration. Results of blood cultures obtained after intermittent antibiotic therapy were negative. However, intensive antibiotic therapy was undertaken by his physician because of presumed bacterial endocarditis. Prophylactic treatment with antibiotics was followed thereafter.

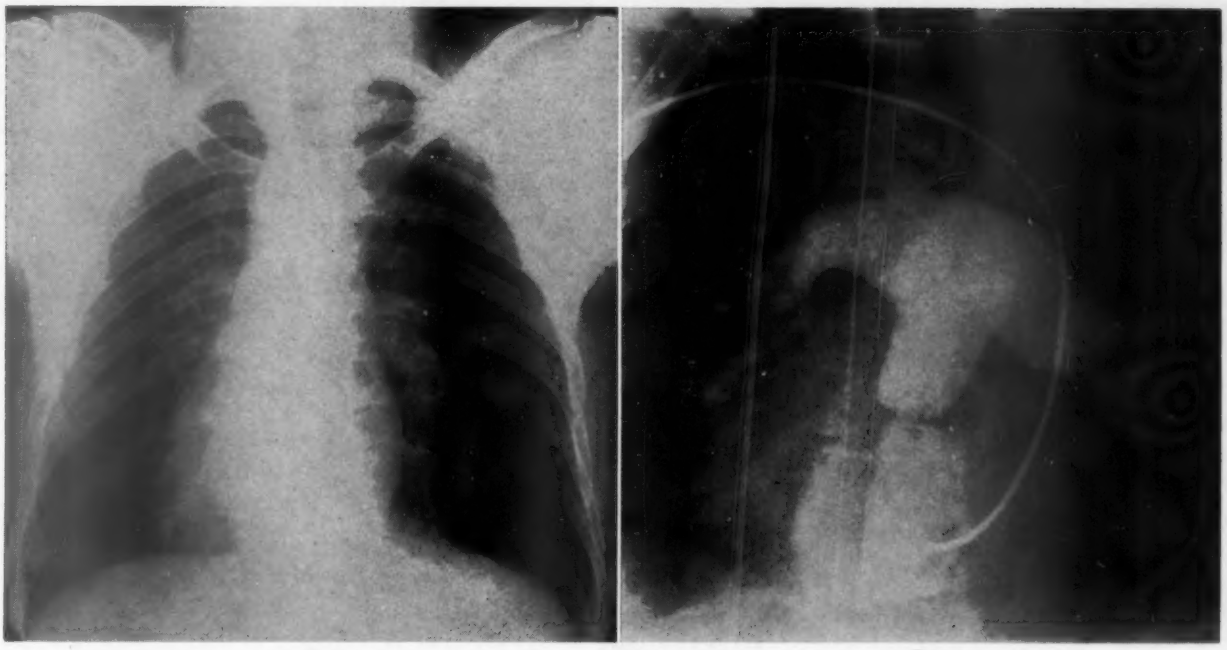
Physical examination revealed mild cyanosis without clubbing. Blood pressure in the upper extremities averaged 125 mm. Hg systolic and 90 mm. diastolic. Pulsations of the peripheral arteries were considered within normal limits. The apical cardiac impulse was on the right and the heart was moderately overactive. A diffuse precordial systolic thrill was most intense parasternally in the right second intercostal space. In the same area a harsh grade 3 (1–4) systolic murmur was heard with transmission posteriorly to the interscapular region. The second heart sound on the right was duplicated and varied in intensity with respiration. The second heart sound on the left was of decreased intensity.

Routine laboratory studies of blood and urine gave normal or negative results. *Roentgenographic studies* of the thorax and abdomen were interpreted as showing complete situs inversus. Except for situs inversus and minor malformations of the ribs, the cardiac silhouette and pulmonary vascular markings appeared to be normal (Fig. 1A). *Electrocardiograms* showed intraventricular conduction defect and "right" atrial and ventricular hypertrophy. *Cardiac catheterization* data (Table 1), dye dilution studies and selective angiocardiography‡ (Fig. 1B) demonstrated corrected transposition with situs inversus, severe

† The present case is referred to as Case 33 in the review by Schiebler and associates.[2]

‡ These studies were made by Dr. H. J. C. Swan.

* From the Sections of Surgery and Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.



A B

FIG. 1. A, roentgenogram of thorax showing dextrocardia and right aortic arch. Note malformations of left first and fourth ribs. B, selective angiocardiogram obtained during cardiac catheterization. An opaque catheter can be seen coursing from a right antecubital vein via the innominate and left superior vena cava and left atrium into the physiologic right (venous) ventricle. Radiopaque dye is seen partially filling the ventricle and pulmonary arteries. The ventricular septum is intact. Note the absence of coarse trabeculation and crista supraventricularis in the ventricle and the extreme narrowing at the usual level of the pulmonary valve. This more caudal and medial location of the pulmonary valve area is characteristic of congenital corrected transposition. Poststenotic dilatation of the pulmonary artery also is apparent.

pulmonary stenosis with poststenotic dilatation of the pulmonary artery, a persistent "left" superior vena cava on the right draining into the venous atrium via an enlarged coronary sinus, and a predominant right to left shunt at atrial level.

TABLE I

Catheterization Data Obtained Seven Months Prior to Operation

Source of Blood Sample	Pressure (mm. Hg)	Per cent Saturation
Radial artery	120/75	90
"Right" ventricle	160/0–10	68–72
"Right" atrium	11/4	75
Inferior vena cava	10/6	74
Superior vena cava	...	68

Systemic blood flow = 2.5 L./min./M.²

Pulmonary blood flow = 1.8 L./min./M.²

"Right to left" shunt = 0.7 L./min./M.² (28% of systemic blood flow)

Surgical Findings and Procedure: On September 18, 1959, under conditions of extracorporeal circulation, the patient underwent open intracardiac repair of the defects associated with the congenital corrected transposition. The heart was exposed through a median sternotomy and the defects were as predicted (Fig. 2). The superior and inferior venae cavae were on the left and there was a persistent right-sided "left" superior cava draining into the venous atrium via the coronary sinus. The aortic arch was on the right. The aorta was anterior and to the right of the pulmonary artery. As anticipated, a coronary artery coursed across the anterior surface of the venous ventricle. A definite thrill was felt over the pulmonary artery, which was dilated. The ductus arteriosus was not patent.

The persistent "left" superior vena cava was safely occluded during the procedure without elevation of jugular venous pressures. The superior and inferior venae cavae were cannulated via the venous atrial appendage, and systemic perfusion was accomplished through a cannula in the right common femoral artery

Because of the expected position of the coronary arteries, it was considered preoperatively that the usual right ventriculotomy incision might not be possible; the pulmonary artery was opened longitudinally exposing an unusually complicated de-

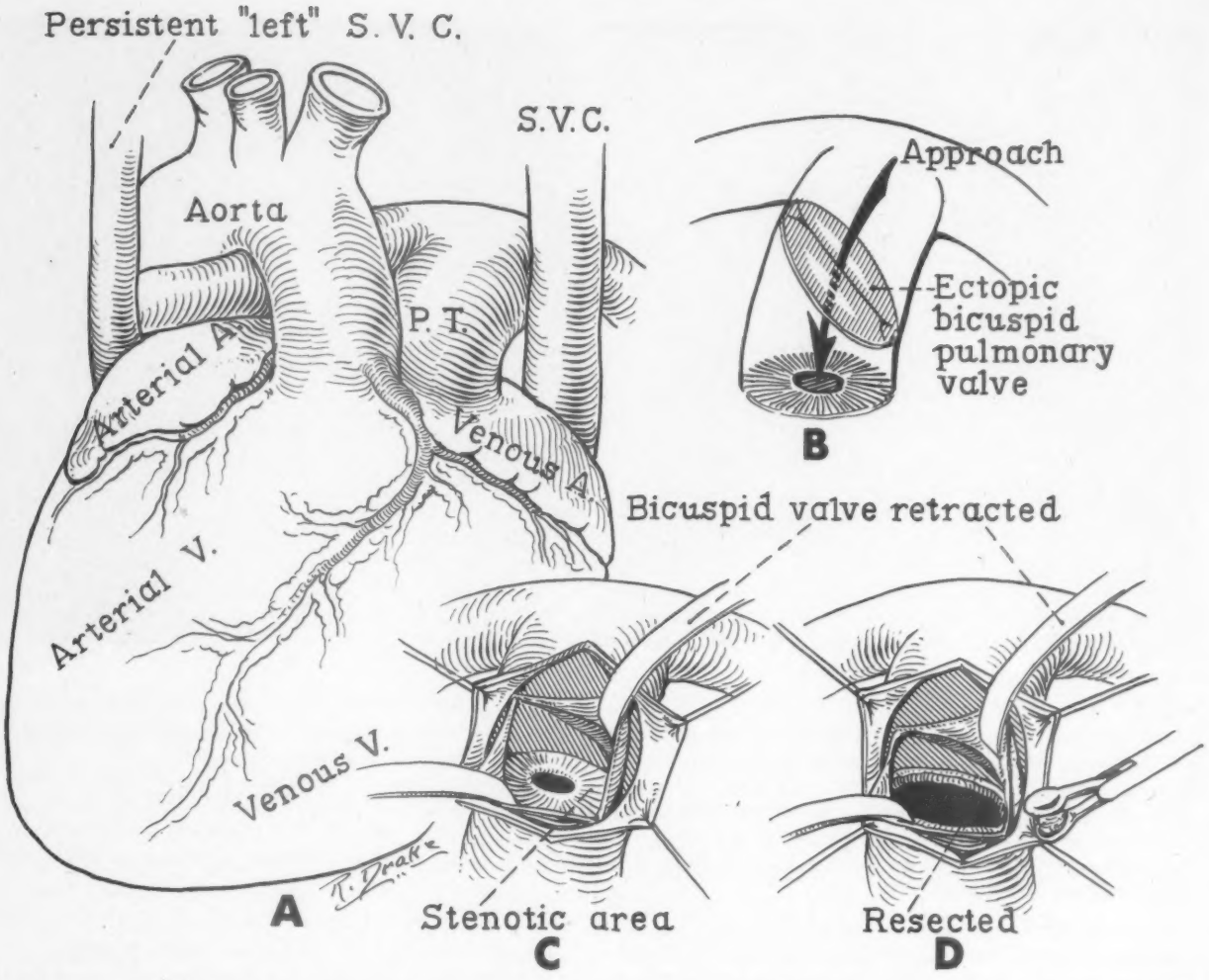


FIG. 2. Appearance of the heart at surgical exploration. A, the physiologic right (venous) atrium is on the patient's left (situs inversus) with the superior vena cava (S.V.C.) and inferior vena cava (not shown) draining into it. The persistent "left" superior vena cava is seen on the patient's right coursing in front of the pulmonary artery on that side to enter the venous atrium behind the heart via the coronary sinus (not shown). Note the right aortic arch, transposition of the aorta and pulmonary arteries and the anomalous coronary artery coursing across the anterior aspect of the venous ventricle. B, transparent drawing of pulmonary artery showing approach from above through the ectopic bicuspid pulmonary valve to the stenotic area below. C, note the cut edges of the vertical incision in the pulmonary artery and the cusps of the ectopic pulmonary valve retracted to expose the stenotic area below. D, similar drawing showing the stenotic area resected.

formity (Fig. 2, inset). Above the pulmonary valve ring and sweeping upward to insert on the right lateral wall of the pulmonary artery were two sail-like obliquely placed valve cusps. The commissure on the left was at a lower level than that on the right. The valve itself apparently did not produce any obstruction. Below the level of the deformed bicuspid valve, at a point where the valve ring is usually located, there was extreme narrowing. Because of the anomalous position of the coronary artery passing across the venous ventricle, repair was attempted through the pulmonary artery. Bulging fibrous tissue on the right lateral wall of this narrowed region resembled a rudimentary cusp. An attempt to excise this unusual mass produced an opening into the outflow tract of the arterial ventricle just below the aortic valve. This surgical defect was closed. It was then only possible to correct the pulmonary stenosis by excising the fibromuscular tissue anteriorly and to the left. Care was taken to avoid re-entering the arterial ventricle or opening through the heart to the outside. With careful dissection it was possible to open the stenotic area from its original 6 mm. to a final opening of 1.5 cm. Muscular hypertrophy was not detectable below the constriction.

The incision of the pulmonary artery was closed with two layers of fine silk. The venous atrium was opened and a valve-incompetent patent foramen ovale measuring 0.8 cm. was closed with a figure-of-eight silk suture. After closure of the venous atriotomy and release of the occlusion of the persistent "left" superior vena cava, the heart was allowed to take over the circulation and extracorporeal circulation was discontinued. The cavae and femoral

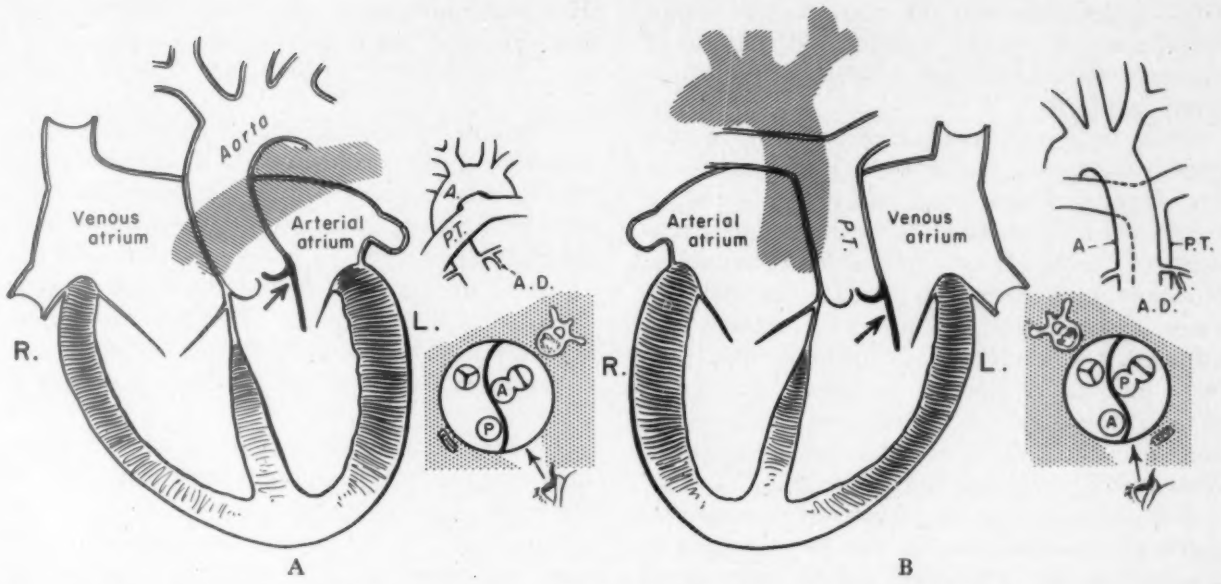


FIG. 3. Schematic illustrations of the essential anatomic features. A, the normal situs solitus heart. B, congenital corrected transposition of the great vessels in situs inversus. In the large diagrams of each panel the more ventral great vessel is shaded. The leaflet of the bicuspid atrioventricular valve in continuity with the semilunar valves is emphasized (arrow): A, shows relationship with the aortic valve; B, with the pulmonic valve. Circular diagrams in lower right of each panel show relationship of ventricular septum and valves to thoracic structures: Cross-section of vertebra is dorsal and sternum is ventral. Heavy black curved line represents the ventricular septum; A represents the aortic valve and P, the pulmonic valve. The atrioventricular valves are shown as bicuspid and tricuspid. The "eye" and arrow at the bottom of each inset show the oblique angle at which the heart is to be viewed to obtain the relationship of the great vessels shown in the inset, upper right. The anterior descending coronary artery (A.D.) is shown arising from the appropriate coronary artery. Note that the anterior-posterior relationship of the great vessels to one another and the proximity of their valves to the atrioventricular valves is reversed in corrected transposition. Furthermore, there is reversal of the superior-inferior relationship of the semilunar valves and adjacent atrioventricular valves. (From: SCHIEBLER, G. L., EDWARDS, J. E., BURCHELL, H. B., DUSHANE, J. W., ONGLEY, P. A. and WOOD, E. H. *Pediatrics*, 27: 851, 1961.[2])

artery were decannulated, the atrial appendage was ligated, the artery was repaired and the incisions were closed with appropriate drainage of the thorax and pericardium. Systolic pressure in the "venous" ventricle prior to repair was 104 mm. Hg while systemic pressure was 75 mm. Hg. After the repair was accomplished, pressure in the "venous" ventricle was 59 mm. Hg and the systemic pressure was 85 mm. Hg.

The patient's postoperative course was complicated by temporary oliguria for three days, probably associated with renal ischemia. Otherwise, the course was uneventful and he returned home twenty-five days after operation. When re-examined five and a half, and eighteen months after operation, he was asymptomatic and renal function was within normal limits.

COMMENT

In congenital corrected transposition of the great vessels the course of blood from the systemic veins through the heart and lungs and back to the systemic arterial circulation is normal in the absence of other defects. The anterior-posterior relationship of the aorta and pulmonary artery is transposed, however, so that the aorta at the root of the heart lies in a plane ventral to that of the pulmonary artery. The coronary arteries arise from the aorta but branch in a mirror-image pattern. The physiologic right (venous) ventricle has the internal architecture of the normal left ventricle, that is, it lies posterolateral to the systemic ventricle, and its internal surface is finely trabeculated, lacks a crista supraventricularis and has a bicuspid A-V valve. The physiologic left (arterial) ventricle, contrary to the usual, lies anterolateral to the pulmonary ventricle and has the internal architecture of a normal right ventricle, that is, it is more coarsely trabeculated, has a crista supraventricularis and possesses a tricuspid A-V valve. Whether situs solitus or situs inversus is present depends on the location of the systemic venous atrium and not on the position of the heart in the thorax (levocardia or dextrocardia). Thus, when the atrium is located on the right, situs solitus exists (Fig. 3A), and when the atrium is on the left, situs inversus exists (Fig.

3B). Levocardia and dextrocardia are minor variations and merely indicate the position of the heart in the thorax without reference to atrial inversion.

Congenital corrected transposition of the great vessels *per se*, in either the situs solitus or situs inversus heart, is not believed to produce significant hemodynamic alteration and is presumably compatible with normal existence. However, most patients with this anomaly have other serious defects which may interfere significantly with function. Ventricular septal defects, pulmonary stenosis or atresia, anomalies of the atrioventricular valves, conduction defects and venous anomalies are frequently associated. Noncardiac anomalies are uncommon.[2]

Surgical treatment for patients with congenital corrected transposition of the great vessels is directed at the associated defects only, since corrected transposition *per se* does not cause disability. Surgical repair of these associated defects may be difficult because of the presence of heart block before and after operation and the persistence of A-V valvular insufficiency not amenable to surgical repair. The anomalous coronary artery pattern interferes significantly with operations requiring reconstruction of the pulmonary ventricular outflow tract for subvalvular stenosis or atresia.

The present case was thought to be favorable for surgical treatment because of the absence of severe heart block, ventricular septal defect or A-V valvular insufficiency. Selective angiocardiography demonstrated the level of the pulmonary stenosis to be valvular and thus potentially correctable without reconstruction of the outflow tract. At operation, however, a complex anomaly was encountered which could have been repaired more easily by reconstruction. However, adequate relief was accomplished from above through the pulmonary artery.

Summary

The case presented, one of corrected transposition of the great vessels with dextrocardia and situs inversus as well as pulmonary stenosis, interatrial communication and persistent "left" superior vena cava, is of interest not only because of the rarity of the condition in situs inversus and the attendant difficulties of surgical orientation but also because the unusual combination of associated defects allowed successful repair.

Surgical treatment for patients with congenital corrected transposition of the great vessels is directed at the correction of associated cardiac defects only, since corrected transposition *per se* does not cause disability. Often the associated defects are multiple and severe, and their repair in the presence of corrected transposition is difficult.

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Diagnostic Shelf

Isorhythmic Dissociation*

LALBHAI M. SANGHVI, M.R.C.P. (London), D.T.M. & H. (England)

Jaipur, India

SEGERS ET AL.[1] suggested that isorhythmic dissociation may be interpreted as synchronization of the beating of atria and ventricles which, however, respond to their own separate pacemakers. Kossmann[2] considered that such electrocardiograms were probably examples of irregular A-V nodal rhythm. Grant[3] explained the A-V arrhythmias, including isorhythmic dissociation, in acute rheumatic fever on the basis of the property of coupled electrical oscillators which tend to pull in or pull apart depending upon their threshold and the rates. Schubart et al.[4] stated that in none of the reported cases of isorhythmic dissociation, including their own cases, can the presence of synchronization be proved and that the mechanism of synchronization still remained in doubt. The purpose of this paper is to present electrocardiograms which may be interpreted as showing synchronization, and other records from the same patient which may help in understanding the mechanism of synchronization in isorhythmic dissociation.

ELECTROCARDIOGRAMS

The electrocardiograms are of a sixty year old man who sustained an anteroseptal and inferior myocardial infarction three months before this examination. Other records of this patient have been reported previously[5] and the patient is believed to have sinoatrial block with shift of the atrial pacemaker, probably to the coronary sinus region in the upper part of the A-V node; the P waves were inverted in leads II, III and aVF. Figure 3 was obtained before and the other figures after administration of bellafolline orally in doses of three tablets daily. The drug was given from April 12 to 16. No digitalis was administered.

Figure 1 shows that, except at two places, the P waves cluster closely round the QRS complexes and precede, merge with, or follow them. The P-P intervals vary between 1.40 and 1.80 seconds with an atrial rate of 33 to 43 per minute. The R-R intervals vary between 1.48 and 1.58 seconds with a ventricular rate of 38 to 42 per minute. The maximum P-R and R-P intervals are 0.21 and 0.22 second, respectively, except at two places where the P waves follow the preceding QRS complexes by 0.24 and 0.28 second, respectively, and are followed in turn by premature QRS complexes at P-R intervals of 0.44 and 0.36 second, respectively.

Figure 2 shows a constant P-R interval of 0.22 second in all cycles except in the second beat in the first strip, the first beat in the fourth strip, and the third beat in the fifth strip, in which the P-R intervals are 0.15, 0.11 and 0.18 second, respectively.

Figure 3 shows incomplete A-V dissociation with ventricular capture beats and first degree A-V block. A long record shows an almost constant internodal interval of 1.76 seconds with a ventricular rate of 33 per minute, and variation of P-P intervals between 1.80 and 2.60 seconds with an atrial rate of 22 to 33 per minute. The shortest P-R interval in capture beats was 0.28 second, and the longest R-P interval preceding the capture beats was 0.92 second.

Figure 4 shows inverted P waves preceding the QRS complexes at a constant P-R interval of 0.22 second, indicating A-V nodal rhythm with first degree A-V block.[6] The heart rate varies between 37 and 44 per minute.

Figure 5 shows prolongation of the P-R interval caused by interpolated ventricular premature beats and supports the assumption of A-V nodal rhythm in this figure and in Figure 4.

COMMENT

Segers[7] attributed synchronization to mechanical or electrical influences of ventricular systole on sinus impulse formation. Also, he showed clearly that when mechanical interaction was eliminated, synchronization could be effected by electrical influences alone. This

* From the Department of Cardiology, Sawai Man Singh Hospital and Medical College, Jaipur, India.

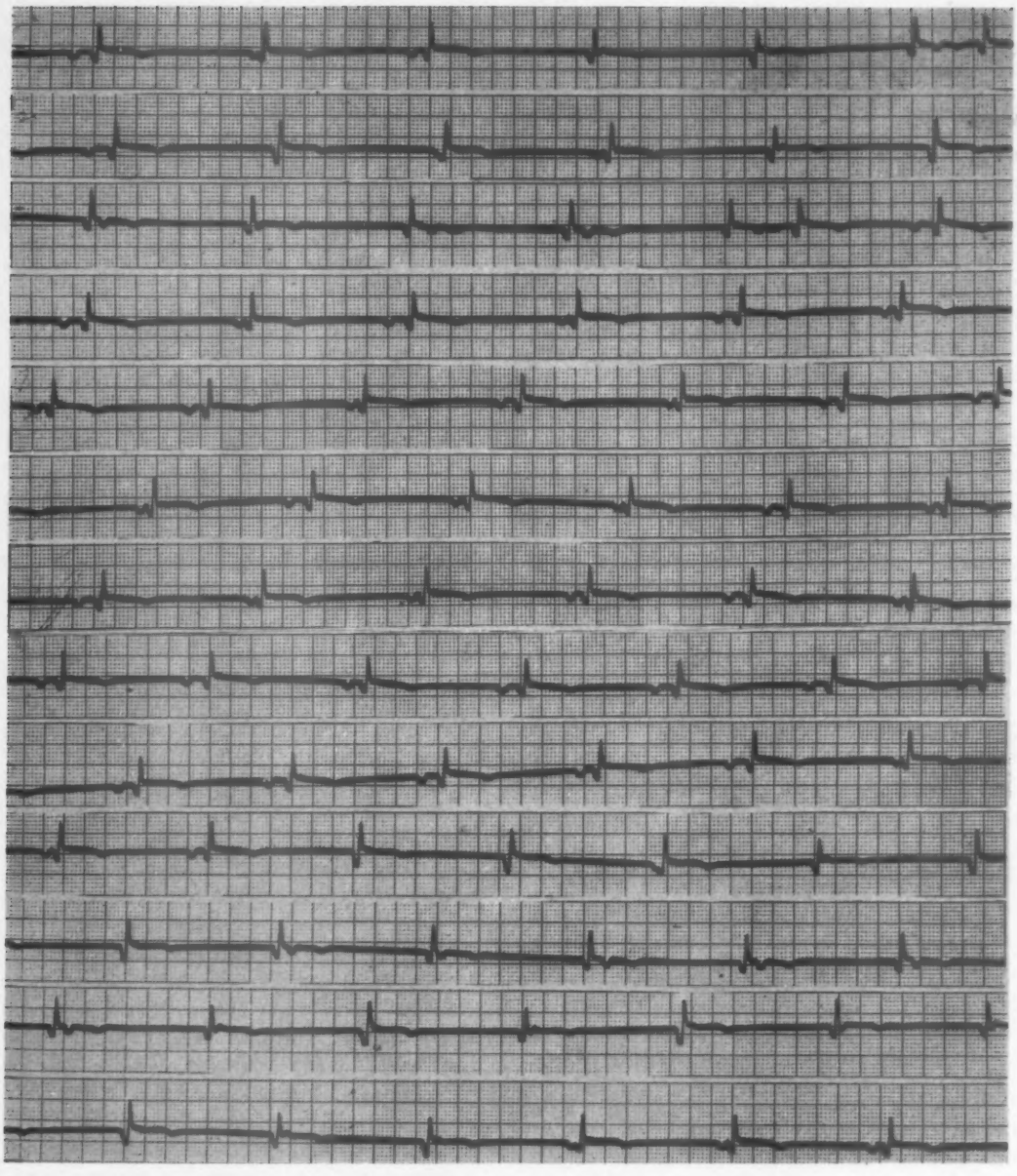

FIG. 1. Lead III. Taken on April 15, 1959, after administration of bellafolline. The strips are continuous.

mechanism, however, does not explain how the P wave can precede the QRS complex in isorhythmic dissociation; it should attach itself behind the QRS. Also, it does not explain the wide variation in the relation of the P wave to the QRS so that sometimes it is in front and sometimes behind the QRS at an interval of as much as 0.24 second as seen in the record of Kossmann[2] and the varying 1:1, 2:1, or 3:1 synchronization in some records in the absence of complete heart block.[8,9] Because rhythmic equality of any two autonomous physiologic foci is difficult to imagine, Kossmann[2] considered the records of isorhythmic dissociation as probable examples of irregular A-V nodal rhythm with varying conduction to atria and the ventricles and sinoatrial block. Lack of negativity of the P waves was considered to be compatible with A-V nodal rhythm.

In the present case Figure 1 is similar to the illustrations of isorhythmic dissociation. Sinoatrial block is believed to be present in this case.[5] Again, in Figure 2 the P-R interval varies in three beats although it is constant in the remaining beats. These findings favor Kossmann's hypothesis of irregular A-V nodal rhythm. If this hypothesis is accepted the two premature QRS complexes in Figure 1

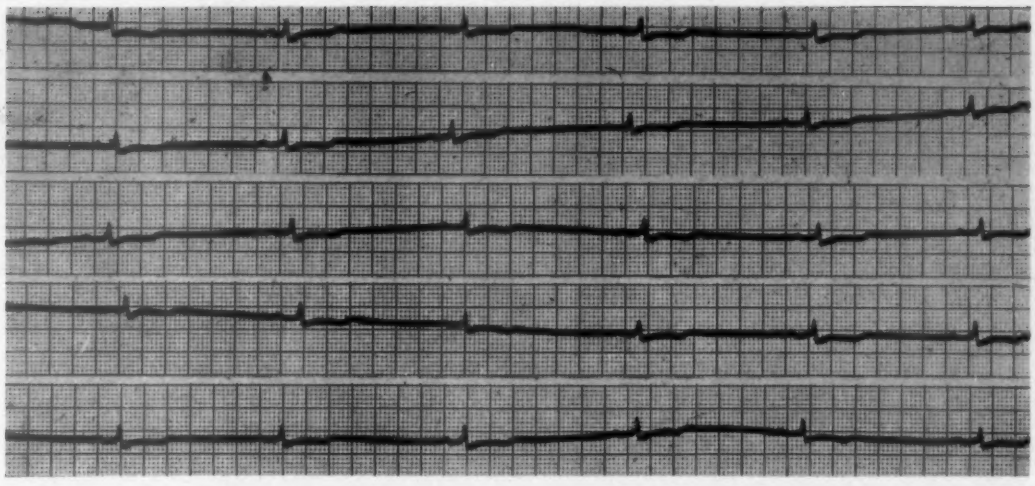

FIG. 2. Lead I. Taken on April 15, 1959, after administration of bellafolline. The strips are continuous.

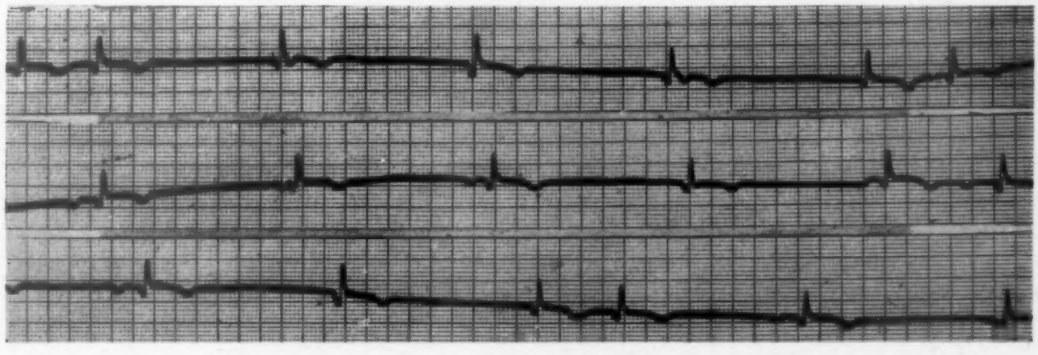

FIG. 3. Lead III. Taken on April 10, 1959, before administration of bellafolline. The strips are continuous.

would represent reciprocal beats. Such an explanation, however, appears unlikely because of the following reasons: (1) A-V dissociation was present when the rates of the pacemakers were slow and the difference between the rates was comparatively greater; (2) A-V nodal rhythm with constant P-R interval was noted in other records which show that the P-R interval does remain fixed when there is A-V nodal rhythm and, therefore, variation of conduction to atria and ventricles of as much as plus 0.21 to minus 0.22 second is less likely to occur with such a rhythm; (3) isorhythmic dissociation occurred only when the rates of the two pacemakers were accelerated after administration of bellafolline, so that they became nearly identical; and (4) significant variation of R-P and P-R interval preceding the premature QRS complexes in the absence of a retrograde Wenckebach phenomenon favors the possibility of ventricular captures rather than reciprocal beats in these complexes.

It can be assumed that the rhythm in the present case became unstable when, after administration of bellafolline, the difference in the rates became much less; thus, in some records there was A-V rhythm and in others isorhythmic dissociation. This instability was also seen when premature beats were followed by change of rhythm from A-V rhythm to isorhythmic dissociation and vice versa.[5] The arrhythmias can be better explained on the analogy of Grant's hypothesis of electronic analogue of the A-V node.[3] When the rates of the two electronic coupled oscillators representing the two pacemakers vary considerably and the rate of P is slower, the slower pacemaker runs free, producing A-V dissociation (Fig. 3). With acceleration of the rates when the difference between the rates of the two oscillators is slight or the rates are nearly the same, the two oscillators representing the pacemakers have a tendency to "pull in" and P waves and QRS complexes cluster together producing isorhythmic

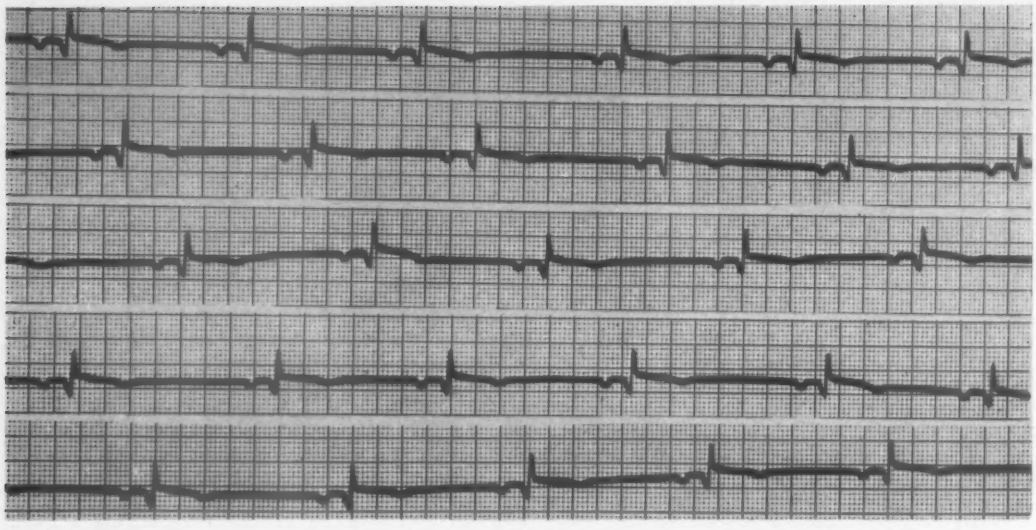

FIG. 4. Lead III. Taken on April 14, 1959, after administration of bellafolline. The strips are continuous.

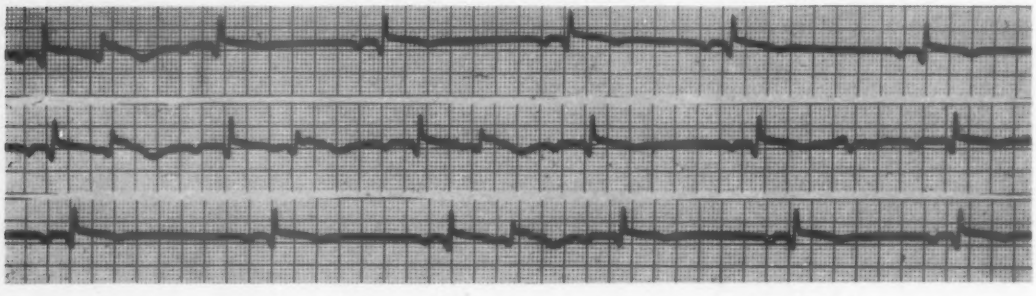

FIG. 5. Lead III. Taken on April 16, 1959, after administration of bellafolline. The strips are continuous.

dissociation. If the rate of the oscillator slows and if the P gets past a little further from the QRS it captures the ventricles (Fig. 1). When the rates are identical they "pull in" as a stable form of operation producing a constant P-R interval (Fig. 4) although occasional slight variation can occur (Fig. 2). The records in the present case, therefore, support the concept of Grant that isorhythmic dissociation is due to a functional disturbance in the A-V node in which the two pacemakers tend to "pull in" because of electrical influences.

SUMMARY

A case is reported whose electrocardiograms may represent a clinical example of isorhythmic dissociation with synchronization.

ACKNOWLEDGMENT

Dr. L. R. Sarin, Superintendent, Sawai Man Singh Hospital, kindly permitted the publication of this report

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Cardiac Resuscitation

Edited by PALUEL J. FLAGG, M.D., F.A.C.C.*

New York, New York

Present Day Cardiac Resuscitation

ROBERT M. HOSLER, M.D.

Cleveland Ohio

FROM TIME immemorial man has courageously attempted some form of resuscitation. It is reasonable to assume that down through the ages, even before written history, there have been numerous and diversified efforts to achieve revival, occasionally resulting in success. In this twentieth century the resuscitation problem is still very much with us.

HISTORICAL BACKGROUND

Probably thumping upon the chest and mouth to mouth respiration are examples of methods of antiquity which have come down to the present day, and they may actually precede the written history of man. The latter method is mentioned in the Bible, II Kings, Chapter 4. This dates it and records it at least some three thousand years ago. It was practiced widely until the sixteenth century when Parcelsus introduced the common fireside bellows as a means of bringing air into the lungs as a less repulsive method. From this time many machines, methods and gadgets were introduced by the ambitious and embryonic profession. Exceedingly few of these have withstood the exacting test of time. Smellie in 1763 described and developed the counterpart of our present day resuscitube.

Although the first successful cardiac resuscitation in the operating room was recorded by Lane in 1902, a queer lack of knowledge persisted and prevailed in medical circles for almost fifty years. In 1947 Beck carried out the first successful treatment of ventricular fibrillation which caused the profession to stir somewhat from its lethargy. Regular postgraduate courses were begun for serious education in respiratory resuscitation by Paluel Flagg in 1947. In 1950, Beck, Rand and I,[1] with the sponsorship of the Cleveland Heart Society, inaugurated what is thought to be the first concerted effort by the medical profession to establish a practical educational program for the prevention and treatment of cardiac arrest. Shortly thereafter Leighninger, Hingson and Mautz joined this pioneering group. This course which began as an orphan has been filling a basic need and has continued on a monthly basis for the past eleven years promulgating itself merely by word of mouth. Considerable progress has been made in the last decade, but the reanimation of people from clinical death is no doubt, as of today, in its infancy.

In Moscow, practical and basic research is diligently pursued on a day to day schedule in the Institute of Reanimation, which is an integral part of the Academy of Medical Sciences of the U.S.S.R. This unique and progressive institute is directed by Professor V. A. Negovsky

* President, National Resuscitation Society, Inc., 2 East 63rd Street, New York 21, New York.

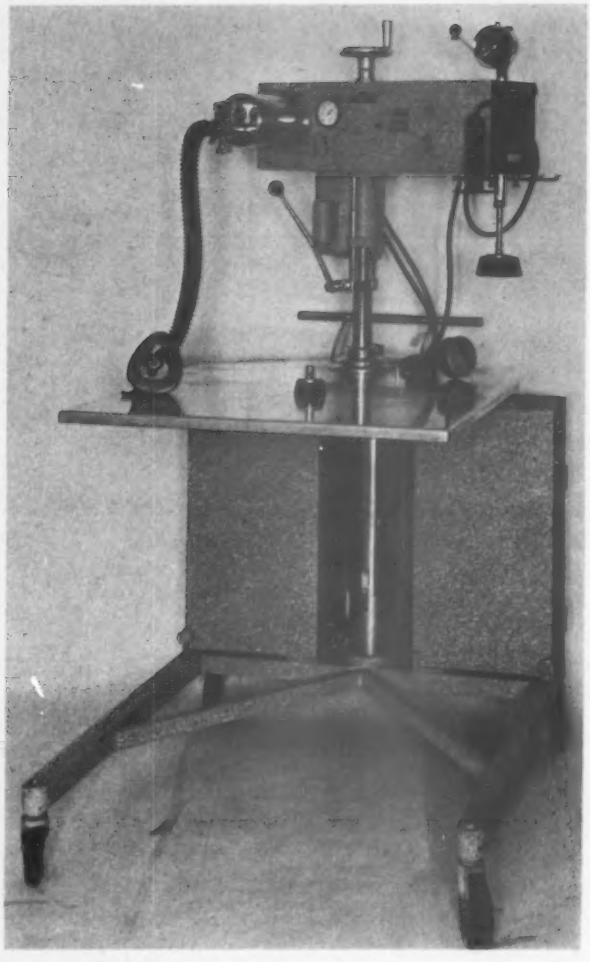

FIG. 1. Beck-Rand heart-lung resuscitator. (Permission of Rand Development Corp., Cleveland, Ohio.)

and his assistant N. L. Gurvich. I have had the good fortune and opportunity of corresponding with these men since 1957 and this brought about my rewarding meeting with this dedicated group in Moscow[2] in 1958.

It is a little over a decade since Beck's successful treatment of ventricular fibrillation, and in 1955 his equally successful reversal of clinical death in a physician with a so-called fatal coronary attack. The subject has subsequently encompassed ever widening horizons. It has naturally been hoped that some practical method will be developed that will prove effective without open chest cardiac massage.

Physiologic Principles

One of several inherent and overlapping properties of cardiac muscle is excitability. It seems that present knowledge of the metabolic process underlying excitability and the response to stimulation is still quite limited. An arrested heart with its oxygen-depleted cardiac muscle will completely lose its excitability in a short time.[3] Although there are many variables, this relatively immovable time limit is around sixty seconds, plus or minus. This significant fact is of singular importance in considering the restoration of the heart beat by physical stimulation, such as pounding upon the chest, the application of a heartpacer stimulus, or the employment of an external defibrillating shock. Some means of reversing this loss of excitability by restoring some degree of cellular metabolism must be provided after this brief time limit. Perfusion of the coronary system with oxygenated blood under a minimum pressure of 40 mm. Hg will sufficiently restore its chemical metabolic energy sources even after many minutes of arrest.

Open vs. Closed Chest Resuscitation

At present there are three practical means for the accomplishment of this: (1) manual open chest cardiac massage; (2) intra-arterial transfusion;* and (3) closed chest transthoracic cardiac massage.

Kouwenhoven, Knickerbocker and Jude[4] have made a great contribution in their development of closed chest transthoracic cardiac massage. Only more experience will indicate whether or not it will meet the exacting and ruthless test of time. Already it has had considerable acceptance and success. Nevertheless, in my opinion its prime application will be in extramural catastrophes, and in emergency situations, both extramural and intramural, needing transportation to a more suitable environment if open chest technic is indicated.

It is only reasonable to state that, with one's hand upon the heart, a more effective circulation can be produced than by the method of closed chest cardiac massage, particularly if the thoracic cage is rather inelastic. Leighninger† states that blood flow studies in a series of dogs reveal that slightly over twice as much blood can be moved by the technic of open chest cardiac massage as by the closed method.

There is no indication or reason to abandon a

* Preferred by the Russian medical profession.
† Personal communication.

method which has stood the test of time. Specifically, it is indicated if the victim is in a suitable place for professional open chest technic, especially if the circulation has not been restored by other methods within thirty to sixty seconds. Upon innumerable occasions in the laboratory during the performance of external defibrillation upon dogs,[5] I have placed the heart in standstill quite readily, but there was no return of the circulation. Upon opening the chest, and manually squeezing the ventricles, the heart beat and circulation were quickly restored.

Of interest to me and Kouwenhoven and associates is the following quote from a reprint of work done in the Institute of Reanimation of the U.S.S.R. by Gurvich and associates in 1945. Space permits only using a few paragraphs taken out of context: "The condenser discharge restored cardiac function if the discharge was applied not later than one to one and one-half minutes after the onset of fibrillation. However, this interval of time does not constitute the limit. By means of preliminary massage of the heart, normal cardiac function may be restored by discharges applied after a rather long period of fibrillation. The heart was massaged by pressure upon the thorax and circulation re-established as shown by pulse waves on a tonograph." In addition, to quote from a letter* from the same institute dated December 27, 1960, referring to closed chest massage: "I know that this method is indeed effective, when used on small children, due to the great elasticity of their thoraces. However, it appears to me that the method does not produce very positive results when applied to grown-ups. One must be certain that one does not merely stimulate weakened heart action."

The Cleveland group has diligently presented and popularized cardiac resuscitation for the past eleven years with the zeal of crusaders. The mood, if such a descriptive term is permissible, of the medical profession can be one of acceptance or nonacceptance. Gradually the soil has become fertile for the acceptance of resuscitation technics. Credit should be given to this deserving group as this subject has obviously been hard to sell. It is apparent that any method which does not necessitate the foreboding task of opening the chest is easy to sell after the soil has become fertile.

Recently a new instrument called a closed chest heart-lung machine was introduced by Beck and Rand (Fig. 1). This machine is so designed that it massages the heart rhythmically by applying pressure of a selected force upon the proper area of the sternum. It also forces air into the pharynx or trachea when the plunger rises. This machine cannot do a better job than the trained pair of hands, but it will not tire out. It could be very effectively used in trained, but not necessarily professional, levels.

Summary

Cardiac resuscitation is still in its infancy as of today. Many hearts will beat again if given a second chance. Kouwenhoven, Jude and Knickerbocker have made a great contribution in this field within the past few months. Their method of closed chest resuscitation can be effectively used in trained, but not necessarily professional, levels. It possibly can save a greater number of lives in the over-all picture as it can have widespread application. The open chest method remains the method of choice in suitable areas in a hospital, as the greatest percentage of lives can be saved with this procedure. In order to prevent the unnecessary loss of life, can we deny that patient the opportunity of a properly executed procedure for open chest cardiac resuscitation? It will be dangerous to preach the abandonment of a method which has already withstood the exacting test of time.

At this critical time it would seem advantageous for a national body such as the National Resuscitation Society to process and digest information and methods, and in turn direct and recommend policy to trained lay groups and hospital staffs.

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* Personal communication.

Progress Notes in Cardiology

Edited by EMANUEL GOLDBERGER, M.D., F.A.C.C.

New York, New York

Dangers of a Low Sodium Diet in the Treatment of Acute Myocardial Infarction*

THE VALUE of restriction of sodium intake in the treatment of patients with malignant hypertension, and the demonstration that decreased renal blood flow, with a retention of sodium and water, occurs in congestive heart failure, has prompted the use of a 500 mg. low sodium diet (which is approximately equivalent to 750 mg. salt) in patients with acute myocardial infarction. Such dietary sodium restriction can be dangerous and even fatal, for the following reasons:

1. The development of acute myocardial infarction is associated with a sudden decreased cardiac output, regardless of whether clinical signs of shock are present. Therefore, one of the aims of treatment is to maintain the cardiac output, especially if the patient shows shock-like signs. For this reason intravenous and intraarterial transfusions have been used, and more recently, norepinephrine, metaraminol and other vasopressor agents have been administered.

2. The osmotic pressure of the extracellular water is determined in most patients by its ion concentration. The cation or anion concentration of the extracellular water is approximately 155 mEq./L. The normal serum sodium concentration is 142 mEq./L., approximately 90 per cent of the total serum cation concentration. Therefore, a decreased serum sodium concentration is associated with a decreased osmotic pressure of the extracellular water. According to the rule of osmotic flow, water will flow from a region of low to a region of high osmotic pressure. Therefore, when the osmotic pressure of the extracellular water decreases, water will flow from the extracellular water into the cells, to equalize the differences of osmotic pressures between these two regions.† As a result, the extracellular water volume and the circulating blood volume will fall. When this occurs in a patient with acute myocardial infarction, shock can be precipitated or aggravated.

3. Sodium loss may not develop at all, even in a patient with myocardial infarction on a low sodium diet, because it is well known that normal persons can withstand sodium restriction for a long period of time without any significant change in serum sodium concentration. However, it has been my observation that many patients in whom myocardial infarction develops have more or less generalized arteriolar changes, particularly in the kidneys. As a result of this, renal tubular function is disturbed and there is a continual loss of sodium into the urine, regardless of the dietary sodium intake. When sodium intake is restricted, a severe sodium loss can occur in 3 to 4 days in these patients.

4. Signs of mild to moderate pulmonary congestion with râles often develop in patients with acute myocardial infarction due to the decreased cardiac output. If such a patient is given an injection of one of the mercurial diuretics, or is placed on oral diuretic therapy with such drugs as chlorothiazide derivatives, such treatment can cause the clinical signs of sodium loss to develop more rapidly.

The physician should be aware of early symptoms and signs of sodium loss such as generalized weakness, apathy, lassitude, anorexia, nausea, vomiting and a loss of skin turgor, even when overt signs of shock are not present.† A marked lowering of serum sodium

† GOLDBERGER, E. A Primer of Water, Electrolyte and Acid-Base Syndromes. Philadelphia, 1959. Lea & Febiger.

* A contribution of the Dr. Louis B. and Anna H. Goldberger Memorial Foundation for Medical Research. Presented at the Hebrew University-Hadassah Medical School Hospital, Jerusalem, April 3, 1961.

concentration is not always present, and I have observed a severe sodium loss syndrome in elderly patients when the serum sodium concentration had decreased only to 135 mEq./L.

Treatment with an increased sodium intake (and temporary water restriction) will cause prompt clinical improvement. If the patient is in shock, one should remember to use vasopressor amines dissolved in dextrose and *saline*, rather than in dextrose in water.

A regular hospital diet contains approximately 2 to 3 gm. of sodium (which is equivalent to 3 to 4.5 gm. salt). Therefore, when the patient is admitted, he should be routinely placed on a regular diet, without added salt on his tray. If he enters the hospital with acute pulmonary edema complicating the myocardial infarction, sodium restriction can be used for 1 to 2 days, along with digitalis if necessary, and other measures to treat the pulmonary edema. Then, the sodium intake can be increased.

Abstracts

Edited by SIDNEY R. ARBEIT, M.D., F.A.C.C.

Jersey City, New Jersey

Ballistocardiograph Research Society*

TRIAXIAL HUMAN BALLISTOCARDIOGRAPHY IN ZERO G ENVIRONMENT. *D. E. Beischer, Ph.D.* and *W. C. Hixson.* U. S. Naval School of Aviation Medicine, Pensacola, Fla.

A study of the feasibility of vector ballistocardiography of a free floating body in zero G environment was presented. The possible use of such measurements in space medicine and space technology were discussed. The relationship between the physical characteristics of the ballistocardiogram at normal and zero G were explored. The zero G system has six degrees of freedom of motion (three linear and three annular).

STUDIES OF THE INSTANTANEOUS ASCENDING AORTIC BLOOD VELOCITY IN INTACT MAN RELATIVE TO THE ACCELERATION BALLISTOCARDIOGRAM. *Samuel M. Fox, III, M.D., J. Richard Warbasse, Raymond B. Crawford, M.D., Joseph C. Greenfield* and *William R. Scarborough, M.D.* Cardiology Branch of the National Heart Institute and the Federal Aviation Agency Research Laboratory, Georgetown University Hospital, Washington, D. C.

The continuous measurement of the instantaneous time-course of blood flow would be of great value to the clinician and investigator and of particular interest for making comparisons with the ballistic movements of the body. A useful approach has been found for the continuous determination of the ascending aortic blood velocity by analogue computation from the spatial differential pressure obtained during retrograde catheterization in intact man. Canine studies comparing the blood velocity (computed from catheter-manometer signals) with an electromagnetic flowmeter in series have strengthened the impression that the clinically well correlated data obtained in twenty-nine human studies are technically valid. There is a direct linear relationship between the acceleration of blood in the ascending aorta and the acceleration ballistocardiogram. Drugs that varied one of these variables varied the other in direct proportion. The technics used and results obtained were illustrated.

AN AIR SUPPORTED BALLISTOCARDIOGRAPH. *Wilhelm E. Rothe* and *Billy O. Martin.* Astro-Space Laboratories, Inc., Huntsville, Ala.

An air supported ballistocardiograph has been developed which appears to have certain unique advantages over more conventional systems. This type of suspension has provided for a virtually frictionless system with a great reduction in the effect of external vibrations and distortions from internal resonances. The need for viscous damping has been eliminated. These factors increase the accuracy and reproducibility of the tracings.

The frequency response of the system is flat to 60 c.p.s. In addition to these factors, this method will allow simultaneous two-axis recordings and gives encouragement toward the possibility of developing a system which will permit measurement of both linear and angular accelerations about the three axes.

THE EFFECT OF INDUCED ANOXEMIA ON THE BALLISTOCARDIOGRAM. *Raymond Penneys, M.D.* Vascular Section, Robinette Foundation, Hospital of the University of Pennsylvania, Philadelphia, Pa.

The ballistocardiogram (high-frequency, Starr type) was taken during the induced anoxemia test, with oximeter-control (*Arch. Int. Med.*, 101: 747, 1958), to see if it would provide additional evidence of coronary insufficiency. The criterion for a "positive" test was an anginal attack or an abnormal electrocardiogram during induced anoxemia. Fourteen healthy, middle-aged subjects and 141 coronary suspects were studied. All healthy subjects had negative tests as did ninety-four of the suspects; forty-seven suspects had positive tests.

The ballistocardiogram of the healthy subjects was always within normal limits on breathing air and remained so when low oxygen was administered. In the coronary suspects having a negative test the ballistocardiogram on air was abnormal in 53 per cent of the cases and on low oxygen in 63 per cent; in those having a positive test the comparable values were 75 per cent and 91 per cent. When the ballistocardiogram was abnormal on air it became more abnormal in 30 per cent of the negative tests and in 58 per cent of the positive tests.

As in the case of the electrocardiogram, the usefulness of the ballistocardiogram in the detection of coronary insufficiency is further enhanced by its use during the induced anoxemia test.

* Annual Meeting, Atlantic City, New Jersey, May 1961.

ISCHEMIC HEART DISEASE AND ACCELERATED CARDIOVASCULAR AGING: A BALLISTOCARDIOGRAPHIC STUDY. *Arthur J. Moss, Lt, MC, USNR.* U. S. Naval School of Aviation Medicine, U. S. Naval Aviation Medical Center, Pensacola, Fla.

Ballistocardiographic evaluation of the cardiovascular aging process in overtly healthy men has been previously reported. The purpose of this study is to evaluate the cardiovascular aging process in a group of men with known ischemic heart disease. Twenty-one men less than 54 years of age with previous myocardial infarctions were studied with the ultra-low frequency acceleration ballistocardiograph. Eighty-one per cent (seventeen of twenty-one) of these cardiac patients had an abnormal ballistocardiogram indicative of accelerated cardiovascular aging. This figure is significantly greater ($p < 0.01$) than the percentage of abnormal ballistocardiograms in an age-matched, overtly healthy male population. The present study appears to indicate a definite association between ballistocardiographic evidence of accelerated cardiovascular aging and ischemic heart disease.

PROGNOSTIC VALUE OF ABNORMALITIES OF BALLISTOCARDIOGRAPHIC FORM AS DETERMINED BY A FIVE YEAR FOLLOW-UP OF 221 HOSPITAL PATIENTS. *Isaac Starr, M.D.* Dept. of Therapeutic Research, University of Pennsylvania, Philadelphia, Pa.

Two hundred and twenty-one hospital patients have been followed for 5 years or longer. The contour of their ballistocardiograms was classified according to degree of abnormality by a scheme reminiscent of, but not identical with, that of Brown. In grade I, the records were normal in contour; in grade II, a majority of the complexes of the respiratory cycle were normal in contour, but a minority were abnormal; in grade III, the majority of complexes were abnormal in contour; in grade IV, the records were so distorted that the individual waves could not be identified with confidence without simultaneous electrocardiogram or pulse record, or even with such aid. Of 103 patients with normal records (grade I), the number of deaths during the 5 year period was ten, while five deaths were expected from the acturarial tables. Among the forty-two with slightly abnormal records (grade II), five died and four deaths were expected. Among the fifty-one with markedly abnormal records, twenty-three died and eight deaths were expected. Among the twenty-five with maximally abnormal records, twenty-two died and three deaths were expected. These results indicate that a ballistocardiogram slightly abnormal in form has no prognostic significance, but when the abnormality is extreme, this has great prognostic significance. Of those with maximally abnormal records only 12 per cent survived for 5 years.

BALLISTOCARDIOGRAM OF THE UNANESTHETIZED DOG. *M. Schwartz, M.D.* University of Pennsylvania, Philadelphia, Pa.

The ultra low frequency ballistocardiogram of the unanesthetized dog was compared with those taken from the same animal under anesthesia (morphine sulfate, nembutal, Dial.—urethane). The use of an abdominal binder will decrease but not abolish the deterioration of the ballistocardiogram due to anesthesia. Administration of a sympathomimetic amine produced the same expected results.

OBSERVATIONS BY AN X-RAY METHOD ON INTERNAL BODY MOVEMENTS RESULTING FROM EXTERNALLY APPLIED SINUSOIDAL FORCES. *John L. Nickerson, Ph.D.* Dept. of Physiology and Pharmacology, The Chicago Medical School, Chicago, Ill.

A method using a form of x-ray kymograph has been developed which enables one to observe the movements of internal areas of the body when the body is acted upon by externally applied sinusoidal forces. Observations enable one to determine the resonance, frequency and degree of damping of various internal structures and also the phase lag between the internal movement and the external movement. Objects on the various internal organs showed resonance (increased coupling) at their natural frequency (about 3 to 4 c.p.s.) with a phase lag as predicted by the conventional mathematics of the situation. The significance of these observations in relation to the ballistocardiograph was discussed.

STUDIES OF THE HUMAN SYSTEMIC CIRCULATORY SYSTEM WITH THE AID OF AN ANALOG COMPUTER. *Abraham Noordergraaf, Ph.D.* University of Pennsylvania Hospital, Philadelphia, Pa.

The set-up of the analog computer that represents the left ventricle and the systemic arteries was described briefly. Some extensions of previously described mathematical relationships, especially concerning the introduction of a new equivalent for the left ventricle, are brought up to date. Measurements of a few abnormalities in the cardiovascular system were elaborated.

DIFFERENTIAL CHARACTERISTICS OF CERTAIN ARRHYTHMIAS BY HGH FREQUENCY DIRECT BODY BALLISTOCARDIOGRAPHY. *Nahum J. Winer, M.D.* Lenox Hill Hospital, New York, N. Y.

The method used is the direct body electromagnetic ballistocardiographic recording acceleration in head-foot direction. To date, consistent differential characteristics of the elements of the initial phase of systole have been essentially unattainable. It is proposed that this method can detect these changes as manifest in arrhythmias. The forms and amplitude of the ballistocardiographic complex in premature beats may be used as criteria of the efficiency of the heart.

FURTHER EVIDENCE FOR THE PROPOSED DIAGNOSTIC CRITERIA FOR MYOCARDIAL INFARCTION WITH DIRECT BODY ELECTROMAGNETIC HEAD-FOOT BALLISTOCARDIOGRAPHY. *Nahum J. Winer, M.D.* Lenox Hill Hospital, New York, N. Y.

The formulation of four characteristic high frequency alterations of the ballistocardiographic pattern in myocardial infarction involving HI, specifically, as a prerequisite for diagnosis is proposed in line with earlier reports. They are: (1) HI deterioration with accentuated isometric contraction—H_{IC}. (2) HI in overall deterioration. (3) HI deterioration with otherwise high pattern amplitudes. (4) HI deterioration with J_R accentuation.

An example of each was presented.

Book Reviews

Atrial Septal Defect: An Investigation into the Natural History of Congenital Heart Disease, by H. Gösta Davidsen. Ejnar Munksgaard, Copenhagen, 1960, pp. 225, O Kroner 50.

This monograph affords detailed analysis of the clinical and anatomic features of 322 cases of atrial septal defect. These consist of 190 postmortem cases derived from the literature and 132 personally observed cases from the Cardiological Laboratory of Copenhagen's Rigshospitalet.

The volume of material alone, placing this among the largest series extant, is enough to make this study of value. In addition, the author has analyzed the case material carefully and has derived considerable information concerning the anatomic varieties of atrial septal defects, coexisting anomalies, mortality rate, hemodynamic alterations, radiologic and electrocardiographic changes and the clinical course.

The book is of the most value in providing data on a large number of patients followed over a period of several years, thirty-six of whom were recatheterized. Some idea of the natural progression of the disease, particularly in regard to changes in the pulmonary vasculature, is thus afforded.

Despite the presentation of considerable data, one area is rather incompletely examined. Although brief mention is made of the effect of surgical closure of the defect on the electrocardiogram, the effects of successful surgery on the numerous other parameters analyzed are not fully discussed.

In the present era of early surgical intervention for atrial septal defect, large series of cases, which permit analysis of the natural history of the disease, will probably not be accumulated in the future. This volume should serve as a valuable reference work in this regard. LESLIE A. KUHN, M.D.

Cardiac Emergencies and Related Disorders, by Harold D. Levine. Landsberger Medical Books, Inc., New York, 1960, pp. 381, $12.00.

This book discusses the common cardiac emergencies encountered in general clinical practice. It includes excellent descriptions of the treatments of acute left ventricular failure, shock, coronary emergencies, acute cor pulmonale, "refractory" congestive heart failure, the various cardiac arrhythmias and cardiac tamponade. In each section the author covers in detail the various drugs indicated, their dosages and mode of administration, and other adjuvant measures, including phlebotomy, oxygen therapy, physical and mechanical measures, etc. The book is highly readable, simply written, informative and should be of greatest value to the busy practitioner and hospital resident physician who are the first ones to be called on to treat these life-threatening emergencies. S. D.

Chemistry of Heart Failure, by William C. Holland, M.D. and Richard L. Klein, PH.D. Charles C Thomas, Springfield, 1960, pp. 116, $5.50.

The authors have succeeded in bringing together in a concise form the salient features of the chemistry of heart failure. The approach to the subject is logical. The concepts of thermodynamics and the work of the heart are discussed. The relationship between the energy production systems of the myocardium and the conversion of chemical energy into mechanical energy are delineated at a cellular and enzyme level. The disturbances of free energy release in the failing heart are considered from the points of view of anoxia, coenzyme lack and hormonal imbalance. Disturbances in free energy utilization are discussed in light of electrolyte metabolism and cardiac hypertrophy.

The effect of the digitalis glycosides on the facets of cardiac energy utilization are delineated from the most recent investigations in this field. Ionic exchange with regard to the cations K^+ and Na^+ and especially Ca^{++} appear to be implicated in the restoration of the hypodynamic heart to normalcy under the influence of the digitalis glycosides.

The authors have clearly and succinctly presented a complicated biochemical phenomenon with a felicity of diction that holds the attention of the reader. The monograph is documented with abundant references.

JOHN C. KRANTZ, JR., M.D.

Congenital Heart Disease. A Symposium at the Washington Meeting of the American Association for the Advancement of Science, edited by Allan D. Bass and Gordon K. Moe. American Association for the Advancement of Science, Washington, D. C., 1960, pp. 364, $7.50.

This is a collection of the papers presented at the symposium held by the Section on Medicine of the American Association for the Advancement of Science in Washington, D. C., in December 1958.

The volume is relatively small for the scope of the field covered, but by precise editing of individual papers a maximum amount of information is imparted. A distinguished panel of authors, composed of active investigators into various aspects of congenital heart disease, maintains a constantly high and informative level in its presentation. The book is divided into four sections, covering the development of the heart and the origins of congenital heart disease, pathologic physiology, diagnostic technics and surgical therapy. The twenty-one chapters range through all these aspects and include, among others, the fetal and neonatal circulation (Dawes, Adams); experimental production of congenital cardiac defects (Wilson); pathologic anatomy of shunts (Lev); pathologic anatomy of pulmonary hypertension (Edwards); use of indicator dilution technics (Wood); use of foreign gas technics (Braunwald); cinecardioangiography (Sones); intracardiac phonocardiography (Lewis); and surgical chapters by Swan, Lillehei, Kirklin and Cooley.

There can, of course, be little fault to find with the individual chapters. The value of this volume to individual reader depends entirely upon how deeply immersed in the field he presently finds himself. Because of the limitations of space and a regrettable time lag between the conference and publication of the volume, certain aspects of the field which have since achieved some attention, such as various technics of left heart catheterization (retrograde aortic or transseptal), selective left ventricular angiography, aortography, the combination of extracorporeal circulation and profound hypothermia are not covered. The chapters concerning surgery are compressed into too few pages to discuss many aspects adequately in this rapidly progressing field. At this date one who has kept up with the literature will recognize much of the data and, indeed, the illustrations presented. For those a little less involved with the field, this volume should serve as a valuable and concise summation of the more important aspects of congenital heart disease.

LESLIE A. KUHN, M.D.

Der Funktionelle Bau der Herzkammern, by Alexander Puff. Georg Thieme Verlag, Stuttgart, 1960, pp. 87, DM 18 ($4.30).

This monograph presents a valuable contribution to physiologic aspects of the anatomy of the heart. The author has combined, sn a critical way, previous observations with his own anatomic and experimental studies. In addition, special attention has been paid not only to the functional structure of both chambers but also to the moderator band and its function. Wide use has been made of modern registration technics, especially cinematography of the action of the heart. Tne experimental section includes investigations into the heart function after severing of one of the bundles of the conductive system. The book is well worth being studied by everyone interested in problems of modern cardiology. The histology of the heart muscle, however, seems to this reviewer to have not received the attention it deserves, and the electronmicroscopy of the heart receives no attention at all.

BRUNO KISCH, M.D.

Index—Handbook of Cardiovascular Agents, Vol. 2, (1951–1955), Parts I and II, by Isaac D. Welt. National Academy of Sciences—National Research Council, Washington, D. C., 1960, Part I, pp. 917; Part II, pp. 649.

These two massive volumes represent a new attempt to "index in depth" more than 27,000 scientific papers published in 400 scientific journals between 1951 and 1960, relating to the cardiovascular effects of clinical agents. The two parts of Volume 2 comprise the years 1951–1955. Volume 1 will include the years 1956–1960 and Volume 3, 1931–1950. The material is indexed under 232 subject headings and subdivisions of these (blood pressure, heart rate, etc.) and under the various chemical headings. The unique feature of the Index is that detailed and informative index entries of two or three lines in length can largely replace conventional abstracts for most research purposes. This project should prove invaluable to all those engaged in physiologic and pharmacologic research in their search for original papers and periodic review of the literature.

S. D.

Rheographie. Eine Methode zur Beurteilung, peripheror Gefässe, by Fritz Kaindle, Kurt Polzer and Felix Schuhfried. Dr. Dietrich Steinkopff Verlag, Darmstadt, 1959, pp. 109, DM 27.50.

Rheography as applied by the authors tries to gain some insight into the circulation of various parts of the body by measuring changes in the electrical conductivity. The difficulties encountered with the method by earlier investigators from changes in skin resistance have been overcome by the use of alternating current and a circuit measuring conductivity of the tissue, i.e., the core in contrast to the skin. The authors demonstrate that electrical conductivity of the core is proportional to the blood volume and changes in conductivity reflect volume changes in the blood vessels of the area measured.

There is a detailed description of the method, including the circuitry, followed by examples demonstrating its practical value in everyday angiology. The authors demonstrate the use of the method in differentiating between organic and functional vascular changes and in evaluating the effect of drugs upon the vessels. They compare the results of their method with oscillometry and illustrate the validity of their method by arteriograms.

The main advantage of the method is its ease of application. It may be applied to any part of the body and in particular to the head, to which the authors devote a special chapter.

The text is profusely illustrated and those who have difficulty in reading the text will easily be able to follow the authors by studying the illustrations only. The booklet can be recommended to all those who intend to add the method to their diagnostic armamentarium.

ROBERT H. GOETZ, M.D.

BOOKS RECEIVED FOR REVIEW

All books received will be acknowledged in this column. As space permits, books of special interest will receive more extensive reviews.

An Atlas of Acquired Diseases of the Heart and Great Vessels, Volumes 1, 2 and 3. Jesse E. Edwards, 1,401 pages. W. B. Saunders Co. Philadelphia, 1961. *$70.00.*

Arteriosklerose. Atiologie, Pathologie, Klinik ind Therapie. G. Schettler, 728 pages. Georg Thieme Verlag. Stuttgart, 1961. *$24.50.*

Cardiac Problems. 144 pages. The Chest and Heart Association. London, 1961. *$3.50.*

Cardiology. An Encyclopedia of the Cardiovascular System. Volume 5. Related Specialty Fields. 597 pages. Edited by Aldo A. Luisada. MGraw-Hill Book Company, Inc. New York, 1961. *$27.50.*

Cardiomyopexy. New Surgical Treatment for Heart Diseases. A. N. Gorelik, C. Lian, L. Thieblot, M. Jacobi, R. Ricciardi and M. Hasclier. 176 pages. The Myopexy Association of The State of New York, 1961. *$5.00.*

Cardiovascular Abstracts I, 1960, Selected from World Literature. Edited by Stanford Wessler. 192 pages. The American Heart Association, Inc. New York, 1961.

Clinical Disturbances of Renal Function. Abraham White. 468 pages. W. B. Saunders Co., Philadelphia, 1961. *$10.50.*

Congenital Malformations of the Heart, Volume 2: Specific Malformations. Revised Edition. Helen B. Taussig. 1,049 pages. Harvard University Press. Cambridge, 1960. *$17.50.*

Hypokinetic Disease. Diseases Produced by Lack of Exercise. Hans Kraus and Wilhelm Raab. 193 pages. Charles C Thomas. Springfield, 1961. *$7.50.*

Management of Hypertensive Diseases. Joseph C. Edwards. 439 pages. The C. V. Mosby Company. 1960. *$15.00.*

Medical Almanac 1961–1962. Peter S. Nogan. 528 pages. W. B. Saunders Co. Philadelphia, 1961. *$5.00.*

Modern Trends in Cardiology. A. Morgan-Jones. 264 pages. Paul B. Hoeber. New York, 1961. *$14.50.*

Prosthetic Valves for Cardiac Surgery. Edited by K. A. Merendino. 586 pages. Charles C Thomas. Springfield 1961. *$8.25.*

Symposium on Coronary Heart Disease. Edited by Herrman L. Blumgart. 154 pages. The American Heart Association, Inc. New York, 1961. *$3.00.*

Symptom Diagnosis, 5th Edition. Wallace Yater and William F. Oliver. 951 pages. Appleton-Century-Crofts, Inc. New York, 1961. *$15.00.*

The Treatment of Hypertension. George Pickering, William Ian Granston and Michael Andrew Pears. 175 pages. Charles C Thomas. Springfield, 1961. *$7.00.*

You and Your Doctor. William H. Potter. 288 pages. Duell, Sloan & Pearce, Inc. New York, 1961. *$5.00,*

College News

PRESIDENT'S COLUMN

The International Circuit Courses

HISTORY IS frequently designated by the periods in which a large community of nations shared not only economy and arms but also a single language which became the standard of written and spoken communication. Such common language communities have generally been characterized by extended periods of peace and the realizations of the glory and security of Pax Roma. This has encouraged attempts in the development of universal languages: Esperanto, interlingua, lingua franca, etc.

A deeper extension of attempts at international communication utilizing the language of the spirit and soul has created theological missions throughout the world and finally, attempts to extend a philosophy of government have been used in the effort to gain an extension of peace.

Our own days have been described as the age of science, and science has become the universal language. Science, however, has practical utilizations, and scientists in disciplines such as physics and electronics would indeed have difficulty in deciding if their language is that of science or of politics or of weapons. To continue this analysis and to seek some basic common denominator which could represent a universal language, one must consider *lingua medica*, the language of medicine. Here seems to be a nearly ideal method of communication; the final objective, the healthy human body, has an unchallengeable international value. The vaccines, the heart operations, the drugs are all peaceful, exportable commodities. The rules of diagnosis, interpretation of data, of dosage, are generally universal. Few other professions communicate so freely, so readily and perhaps so honestly.

One could extrapolate this basic idea at some length and the reader undoubtedly has. I am also aware of the criticism of naïveté and the need to remind ourselves that the world's problems may be little changed by what we do. Such is not an acceptable end to the discussion, however. There is, and there will always be, a need for ideas and experiments based only upon a belief in good, in altruism, in freedom from bias. Such is a description of the obligation of the physician and of organizations of physicians. It is with this reasoning that the American College of Cardiology is entering into the international field of medical education. Through our Workshops, we intend to develop *International Circuit Courses* and through *lingua medica* communicate with those throughout the world who, like ourselves, carry the designation: Doctor of Medicine. This will require careful planning, hard work and time for maturation. In the next few months our first group will be going out. From this beginning we will get an idea of the problems involved and the good to be done. If this proves useful, many of you will be involved in the future developments. I would appreciate hearing ideas and suggestions from you concerning the concept of the International Circuit Courses.

E. GREY DIMOND, M.D.
President

The Young Investigator's Award for 1961

At the Tenth Annual Convention held at the Hotel Biltmore in New York this past May, the College for the first time in its history offered an award to encourage the young investigators in cardiology; the announcement was made rather late in the year and the deadline was uncomfortably close and yet the response was particularly gratifying. There were twenty-six papers submitted, and a screening committee under the chairmanship of Simon Dack, with the help of Hubert Mann, Henry I. Russek and Philip Reichert, had the unenviable task of selecting the ten papers that would be presented in the final round of the competition at the annual meeting.

The ten papers that were eventually judged to be most original in method, relevant to cardiology in scope and excellent in organization and presentation were the following:

J. David Bristow, M.D., University of Oregon Medical School, Portland, Oregon. "Observations with the Frank System of Vectorcardiography in Left Ventricular Hypertrophy." Introduced by Herbert E. Griswold, M.D.

Abraham Guz, M.D., University of California Medical Center, San Francisco, California. "Simultaneous and Continuous Measurements of Right and Left Ventricular Stroke Volumes in the Conscious Dog." Introduced by J. H. Comroe, Jr., M.D.

P. B. Lambert, M.D., Beth Israel Hospital, Boston, Massachusetts. "The Refractory Period of Ventricular Myocardium as Function of Its Blood Supply." Introduced by Howard A. Frank, M.D.

Jack Lieberman, M.D., Veterans Administration Hospital, Long Beach, California. "Dissimilar Protease Activities of Human Serum." Introduced by R. W. Porter, M.D.

D. M. Long, Jr., M.D., University of Minnesota, Minneapolis, Minnesota. "Myocardial Necrosis and Electrocardiographic Changes Related to Microcirculatory Abnormalities." Introduced by E. B. Brown, Jr., M.D.

Jere H. Mitchell, M.D., National Heart Institute, Bethesda, Maryland. "The Transport Function of the Atrium." Introduced by S. J. Sarnoff, M.D.

M. S. Spach, M.D., Duke University Medical Center, Durham, North Carolina. "Circulatory Dynamics and the Effects of Respiration during Ventricular Asystole in Dogs with Complete Heart Block." Introduced by Jerome S. Harris, M.D.

Mario R. Testelli, M.D., Institute Nacional de Cardiologia, Mexico D.F., Mexico. "Bilateral Bundle Branch Block." Introduced by Demetrio Sodi-Pollares, M.D.

E. Senderoff, M.D., Mount Sinai Hospital, New York, New York. "The Effect of Cardiac Irradiation upon Myocardial Vascularity." Introduced by Samuel H. Klein, M.D.

Paul Nonkin, M.D., Veterans Administration Hospital, Coral Gables, Florida. "The Use of Digitalis in Chronic Complete A-V Heart Block: A Critical Experimental Study." Introduced by Fred Wasserman, M.D.

All these ten men appeared at the Meeting and presented their papers in a special session on Wednesday morning, May 17th. The committee of judges was headed by George R. Meneely, with the help of Clarence M. Agress and Travis Winsor. The session was well attended, especially by that group of the Fellows who are themselves directors of research programs in the various institutions of the United States and Mexico. Each presentation was rigidly limited to ten minutes, including lantern slides. Discussion and questions were limited exclusively to the committee of judges.

The judges then retired for their deliberations, each with his own notes. The voting was remarkably consistent, and during the Convocation on Friday evening when the honors and certificates are awarded annually, Chairman Meneely handed Dr. Bishop the sealed envelope containing the awards.

Dr. Jere H. Mitchell of the National Institutes of Health was named "Young Investigator for 1961" and received a silver medal, a certificate and a check for $1,000.

Dr. D. M. Long, Jr. of the University of Minnesota was runner up, and he received "Honorable Mention" and a check for $200.00.

The Roche Laboratories, who had made an original grant for the award, generously gave each of the other eight contestants a check for $100.00 as a consolation prize because they had survived to the last round of the contest.

The success of the first Young Investigator's Award competition has encouraged the Trustees to make this an annual event and this issue of the Journal contains an announcement for next year's Award (see page 16).

Dr. Graybiel (left) receives the Liljencrantz medal from Dr. C. I. Barron, awards chairman.

Dr. Graybiel Earns Liljencrantz Award for Studies in Space Medicine

CAPTAIN ASHTON GRAYBIEL, MC, USN, Past President of the College and a foremost research specialist in aviation and space medicine, was presented the 1961 Eric J. Liljencrantz Award of the Aerospace Medical Association for his studies on the physiologic effects of space flight. Dr. Graybiel, director of research at the Naval School of Aviation Medicine in Pensacola, Florida, is the creator of the "slow rotation room" which simulates stress and conditions expected to be encountered if orbiting vehicles are rotated to generate an artificial field force. Dr. Graybiel, who has specialized in aviation and space medicine since entering military service in 1942, constructed the "slow rotation room" around the center post of the Pensacola human centrifuge. The room is nearly circular, windowless and is fifteen feet in diameter and seven feet high. The angular velocities used are in the range of the speed of rotation of manned radar platforms and in the range contemplated if inertial field forces are to be generated in orbiting satellites. His work is of theoretical importance for elucidating certain neurophysiologic mechanisms. Dr. Graybiel's procedures can be applied in the selection, indoctrination and preconditioning of space personnel and bear on studies of the cause and control of motion sickness.

PUBLISHER'S INFORMATION PAGE

The Editors and Publishers of THE AMERICAN JOURNAL OF CARDIOLOGY welcome concise articles on new findings in cardiology. As is customary in professional publications, statements in articles are the responsibility of the authors; articles must be contributed solely to THE AMERICAN JOURNAL OF CARDIOLOGY; material is copyrighted and may not be reproduced without permission of the publishers.

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Preparation of Illustrations

So that your article will be presented most effectively, illustrations must be glossy prints or professional drawings in black ink (never in blue; it will not reproduce well). All printing on illustrations should be done professionally or with heavy type. Reference to all illustrations should be inserted in the text in consecutive order. Please follow these identification instructions: Write the figure number and the author's name on the back of each illustration and indicate the top.

Type legends for illustrations on a separate sheet with numbers corresponding to those on the photographs or drawings. Please do not attach legends to the pictures.

A reasonable number of illustrations are supplied free of cost; we know the authors will understand that special arrangements must be made with the publishers for excess illustrations and tables.

Reviews, Abstracts

Books for review may be sent directly to the Editor, Simon Dack, M.D., **The American Journal of Cardiology,** 466 Lexington Avenue, New York 17.

Permission to abstract must be obtained from the publisher. Only paid circulation journals will be permitted to abstract.

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references: (1) Hirshleifer, I.: Adjunctive therapy in cardiacs, presented at the Spring Scientific Symposium, Connecticut Acad. Gen. Pract., Hartford, Conn., March 16, 1961. (2) Fronman, I. P.: The Alleviation of Stress in the Elderly Cardiac Patient, **ibid.** (3) Kent, E. A.: Management of the Hyperactive Geriatric Patient, **ibid.**

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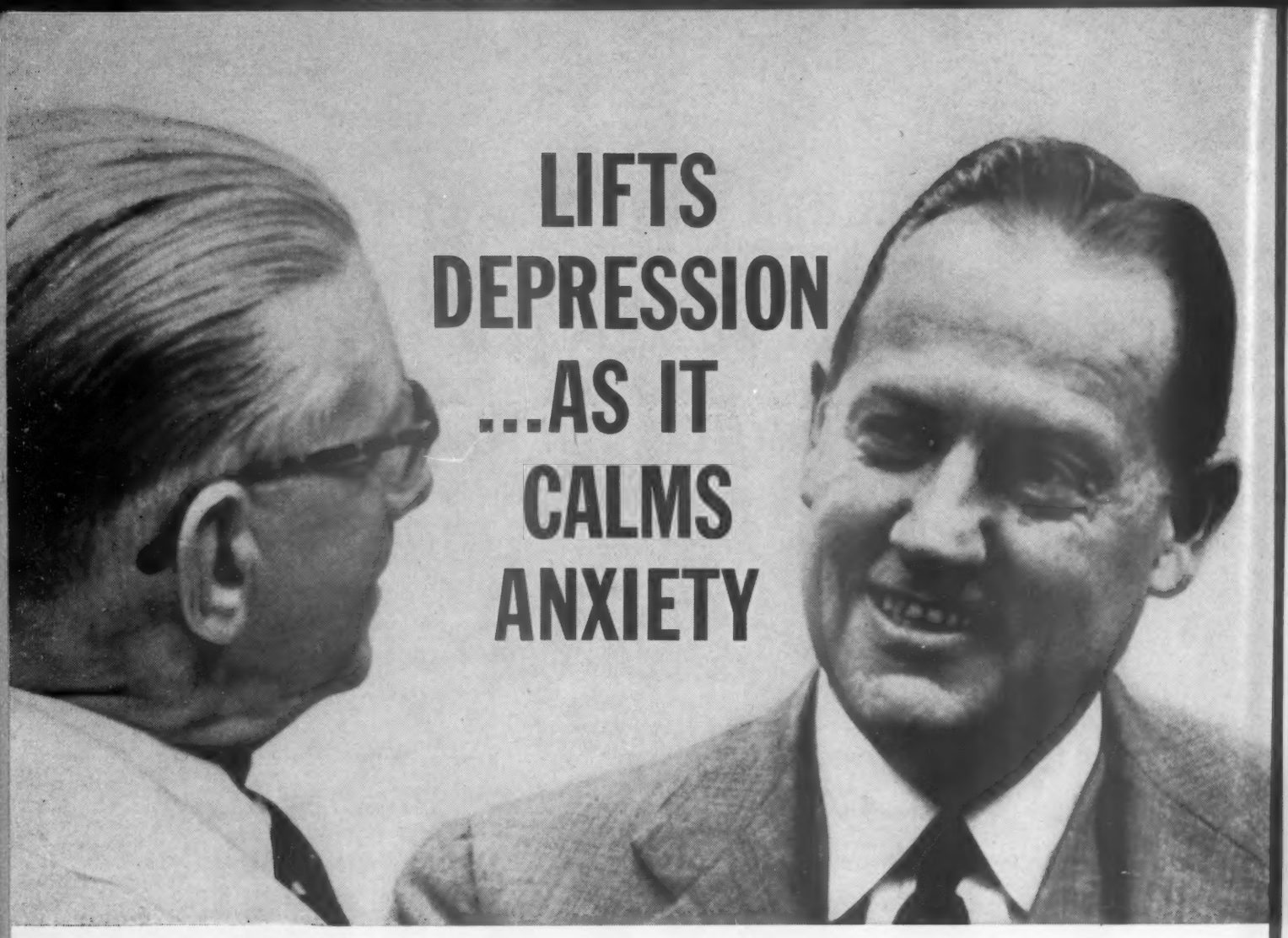

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S. B. SALVIN, PH.D., *Hamilton, Montana.*

From the U.S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, National Institutes of Allergy and Infectious Diseases, Rocky Mountain Laboratory, Hamilton, Montana.

The Course and Prognosis of Histoplasmosis.

HARRY RUBIN, M.D., MICHAEL L. FURCOLOW, M.D., *Kansas City, Kansas,* J. LEWIS YATES, M.D. and CHARLES A. BRASHER, M.D., *Mount Vernon, Missouri.*

From the Kansas City Field Station, Communicable Disease Center, Bureau of State Services, Public Health Services, U.S. Department of Health, Education, and Welfare, University of Kansas School of Medicine, Kansas City, Kansas, and the Missouri State Sanatorium, Mount Vernon, Missouri.

Aspergillosis. A Review and Report of Twelve Cases.

SYDNEY M. FINEGOLD, M.D., DRAKE WILL, M.D. and JOHN F. MURRAY, M.D., *Los Angeles, California.*

From the Department of Medicine, Wadsworth Hospital, Veterans Administration Center, Los Angeles, and Department of Medicine and Pathology, University of California Medical Center, Los Angeles, California.

The Use of Amphotericin B in the Treatment of Coccidioidal Disease.

WILLIAM A. WINN, M.D., *Springfield, California.*

From the Department of Medicine, Tulare-Kings Counties Hospital, Springville, California.

North American Blastomycosis.

E. RICHARD HARRELL, M.D. and ARTHUR C. CURTIS, M.D., *Ann Arbor, Michigan.*

From the Department of Dermatology, University of Michigan Medical Center, and the V.A. Hospital, Ann Arbor, Michigan.

Cryptococcosis (Torulosis). Current Concepts and Therapy.

M. L. LITTMAN, M.D., PH.D., *New York, New York.*

From the Departments of Microbiology and Medicine, the Mount Sinai Hospital, New York, N. Y. These studies were supported in part by research grants from the Squibb Institute for Medical Research and the National Science Foundation.

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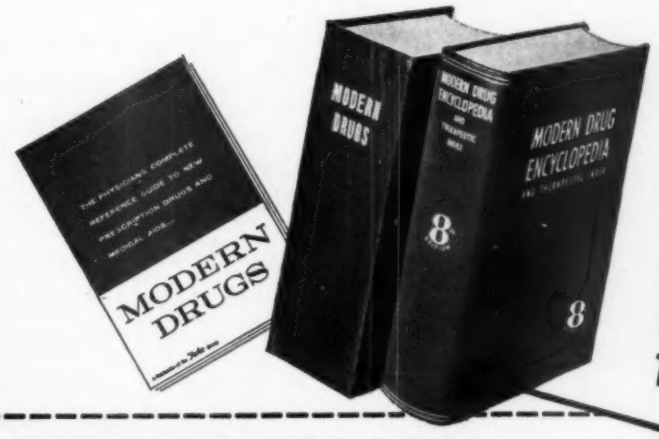

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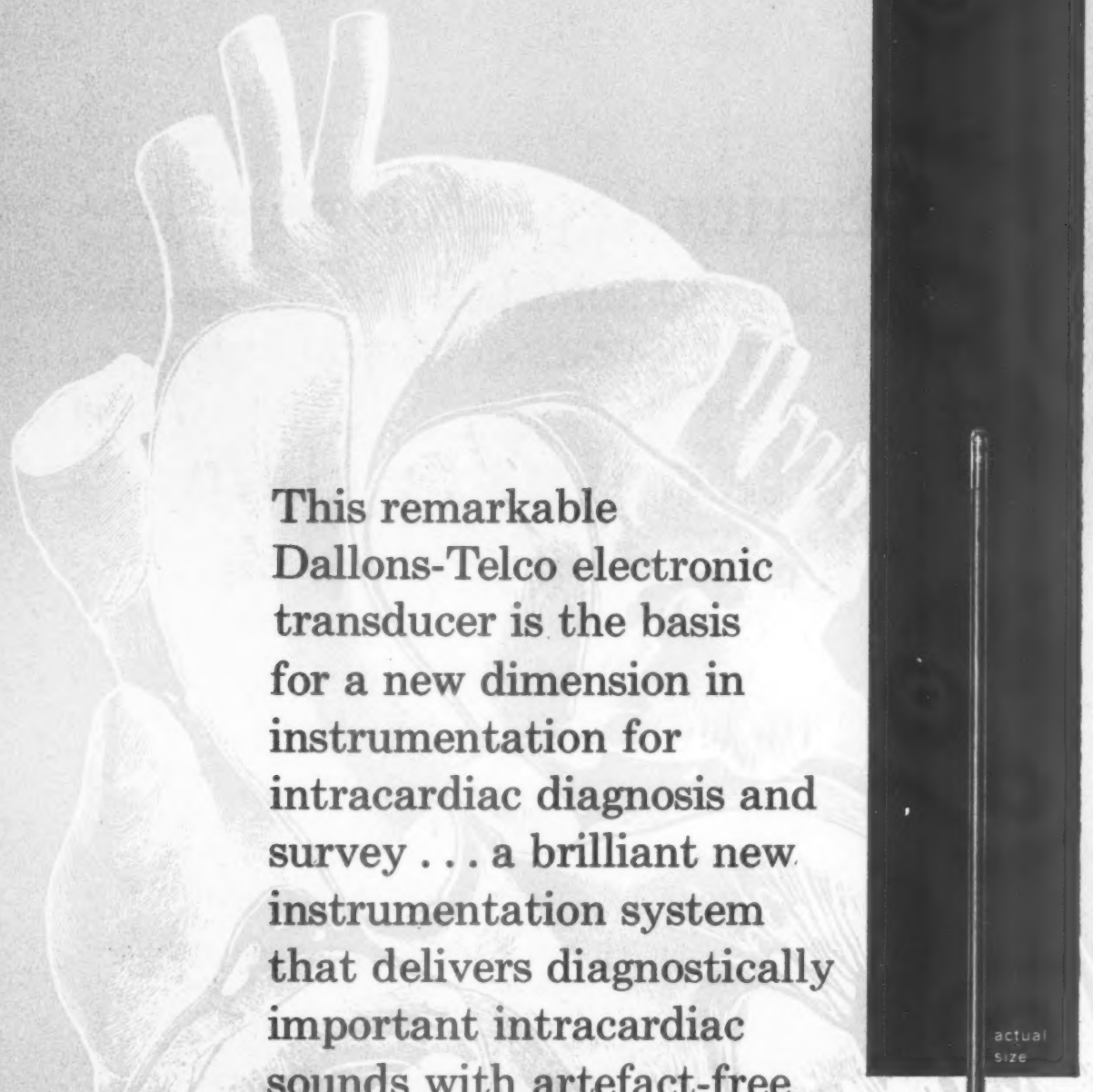

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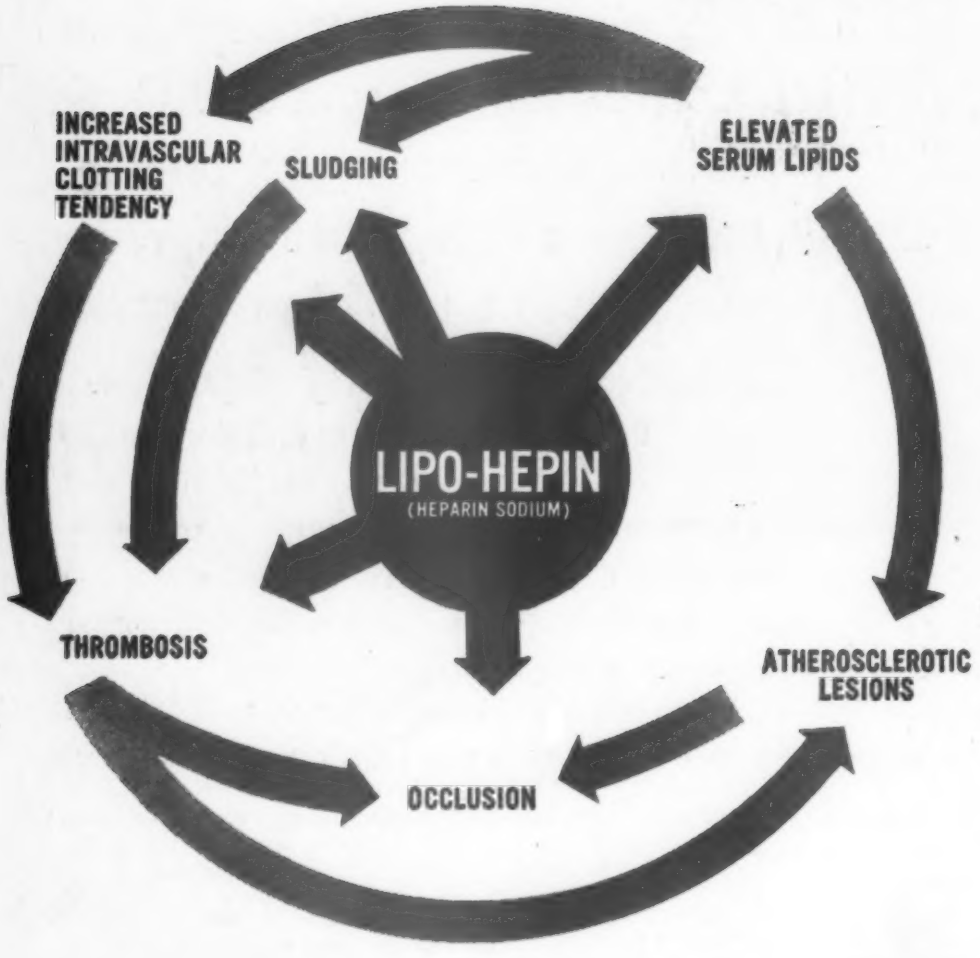

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